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THE PRACTITIONER

No. 778 APRIL 1933 Vol. CXXX

ANÆSTHETISTS AND ANÆSTHESIA: A GENERAL REVIEW

By CECIL HUGHES, O.B.E., M.B., B.S.

Senior Honorary Anæsthetist and Lecturer in Anæsthesia, King's College Hospital; Consulting Anæsthetist, Bethlem Royal Hospital.

THE art and practice of anæsthesia have advanced and changed very considerably during the last few years and have thus rendered possible the great advance in modern surgery. Indeed, it may be truthfully stated that modern surgery entirely depends upon the modern anæsthetic and the complete reliance and confidence of the surgeon in his anæsthetist.

No longer does it suffice for the anæsthetist to pack his Clover inhaler, gas cylinders, mask, lint, ether, and chloroform together, and lightheartedly start out just before the appointed hour. An anæsthetic requires, even for the simplest operation, a certain amount of preliminary consideration and discussion not only with the operator but also with the patient and possibly his relatives. The close co-operation of surgeon and anæsthetist is essential not only in the actual operation but also in the careful preparation and thought necessary to secure the best results in the complicated technique of a modern operation. Very often the patient is neither ignorant of nor indifferent to the subject of anæsthesia, and frequently takes a lively interest in the choice and manner of induction. He may even suggest the particular method and drug he prefers, possibly from previous experience, or from hearsay knowledge derived from friends or relatives, and it is only right that within certain limits his wishes should be met, provided they are not contra-indicated for some sound reason on medical or other grounds.

The surgeon may have very decided views both as to the choice and technique of the anæsthetic. Unless he knows his anæsthetist, he may deem it wiser to allow him to follow his usual practice rather than to insist on others in which he might be less skilled. But in special operations, e.g. of the head, neck, or thorax, the anæsthetic and apparatus used must of necessity conform to the surgeon's demands and methods. The anæsthetist is present primarily as an assistant to the surgeon. As such, a knowledge of the operator and his idiosyncrasies should be a very important guide in regulating the depth of anæsthesia; for surgeons vary considerably as to the degree of abdominal relaxation required. When manipulations and retraction are carried out with gentleness, and the intestines not unduly exposed and kept warm, the task of the anæsthetist in protecting the patient from shock is much easier. Whether five or forty-five minutes are taken to reach the peritoneum, whether the pharynx is kept clear of blood during a tonsillectomy, or the patient is allowed to bleed freely in a breast amputation, would certainly affect the degree of anæsthesia maintained. For there can be no doubt (excluding nitrous oxide) that, given a satisfactory anæsthesia, the less anæsthetic a patient receives the less will he suffer from after-effects.

It has often been stated that there is danger in " light anæsthesia." This needs some qualification, and if " inadequate " or " incomplete " is substituted for " light " few will disagree. The " pseudo or sleepy anæsthetic stage," described by the late Sir Frederick Hewitt, in which it is sometimes assumed that the patient is well under, although probably only in the first or early second stage, is not *surgical* anæsthesia. Vigorous muscular reflex produced by the incision will soon prove that it is very inadequate, and danger from vagal inhibition is quite possible. But a degree corresponding to the early third stage, in which the pupil is small although the corneal-lid reflex is brisk, and in which the incision will only evoke the merest trace of reflex movement will often give perfect and safe anæsthesia, followed by no ill-effect or even knowledge of having had an anæsthetic. The anæsthesia of nitrous oxide and oxygen, when given alone, certainly gives no greater depth of anæsthesia than this, yet here the question of danger of light anæsthesia never arises. That such anæsthesia can also be provided by mixtures of ether and chloroform every anæsthetist of experience will agree.

The great art in anæsthesia is to satisfy the surgeon's requirements with the minimum amount of anæsthetic. This is much easier with mixtures than with open ether, as the adjustment of depth is much finer with the former, while the latitude of safety with ether is much greater, and the finer levels of anæsthesia more difficult to maintain. The younger school of anæsthetists have never been brought up on, and never acquired, the knack of easy induction with the nitrous oxide-ether sequence with the Clover inhaler. Properly given, this sequence is the pleasantest, easiest and most satisfactory form of general induction we possess. But to be perfect, it requires a high degree of skill only acquired by long and continuous practice. An easy and skilful induction is likely to be followed by satisfactory anæsthesia; but if this is badly managed, respiration may well be troublesome, and quiet relaxation difficult to obtain. But perhaps it is in the management of the air-way that an indifferent anæsthetist is most frequently lacking. The vital importance of a perfect air-way, the maximum possible in every patient, is constantly overlooked. The patient is allowed to breathe in a stertorous manner; there is partially obstructed breathing which may soon be followed by deficient oxygenation, congestion, salivation, and the whole vicious sequence. Even if present in a slight degree only it may impair muscular relaxation, and mar recovery by headache and heaviness.

The consciousness of the induction of an anæsthetic is frequently looked upon as an ordeal to be avoided, even by adults. And it is undoubtedly expedient, at times, to spare young children the knowledge of an impending operation or anæsthetic. In either case this can be met by one of the various hypnotics. But in the absence of any distinct indication, it may be questioned if the routine use of hypnotics, particularly for children, would not do away with a small, but valuable, incentive to bravery and fortitude.

The aim and object of producing a perfect anæsthesia with maximum safety, without subsequent sickness or other ill-effects, is always before us. This perhaps is more nearly achieved than ever before by the greater knowledge and the largely increased use of nitrous oxide and oxygen. Numerous improvements in the various gas-oxygen machines, the fine adjustment valves, and the accurate devices for measuring and varying the proportions, with or without ether and (or) chloroform vapour, have greatly facilitated and improved anæsthesia. The gas supplied is free of moisture, thus eliminating the freezing of valves and the necessity for warming them.

The work of Haldane and Yandell Henderson on carbon dioxide drew attention to the practical use of this gas in anæsthesia. When 5 to 10 per cent. is inhaled with air and oxygen well-marked stimulation of respiration occurs. In the induction stage, especially when respiration is irregular, or depressed by sedatives, it will hasten anæsthesia; it tends to abolish "stridor," and in surgical shock it raises the blood pressure, and causes well-marked improvement by deepening respiration. At the end of anæsthesia, by stimulating respiration, the elimination of the anæsthetic, and recovery, are accelerated, and the chances of sickness reduced. It is now recognized that, though gas and oxygen is an excellent anæsthetic for trivial operations and the least toxic in existence, for surgical purposes it is quite useless without the assistance of a hypnotic or basal anæsthetic, or without the use of *some* ether or chloroform.

Ethylene has not been used to the same extent in England as in America. It is claimed to produce greater relaxation than nitrous oxide, and can be combined with a larger percentage of oxygen, but its very unpleasant odour and the great danger of explosion will certainly prevent its adoption in this country. Premedication has recently received much impetus from the discovery of numerous synthetic drugs possessing sedative and hypnotic properties. Looking back for the last thirty years, perhaps the greatest advance has been the use of atropine, which has now become universal. Without it the free and full use of ether would be impossible, and the old picture of a blue face and frothing at the mouth would still be in evidence.

The addition of a small sedative dose of morphine developed into a hypnotic dose of scopolamine. This again has given way to the production of a full and deep hypnotic state to which the term " basal anæsthesia," or " hypnosis " has been applied. Among the drugs commonly used are avertin and many of the barbiturate group, such as nembutal, sodium amytal and pernocton. They are variously given per rectum, by mouth, or intravenously. This is not a new method, as sometimes assumed, for allied drugs, hedonal and isopral, were also given intravenously in thousands of cases before the war. Whether these drugs have come to stay still remains to be proved. It should be realized that they are not true anæsthetics, and if attempts are made to use them as such, disasters must follow. Avertin, which is being extensively given, followed by gas-oxygen and light ether, usually produces a very satisfactory anæsthesia, after-pain being diminished and vomiting negligible. It is liable, however, to cause a fall of blood pressure and, like chloroform, appears to be capable of toxic action on the liver. Nembutal, when given by mouth is more uncertain and does not produce such a deep hypnosis, but intravenously the effect is profound and immediate. Speaking generally, there is no one method of basal narcosis which is universally applicable. The basis of dosage, namely, body weight, does not allow for idiosyncrasy; no reduction or withdrawal is possible when once given, and the respiratory and vasomotor centres may be seriously depressed. Moreover, the results claimed have by no means been uniform, and there are already signs of a consensus of opinion against the intravenous administration of the barbiturates.

Rectal-oil-ether and paraldehyde have both been used as basal hypnotics for a considerable time. With quite adequate dosage, they are perfectly safe and practically non-toxic. The former in addition has the advantage of being an anæsthetic, although the hypnotic state is not reached so rapidly as with avertin and the barbiturates. But when attained, a very satisfactory anæsthesia can be maintained with gas and oxygen, or very light ether, chloroform or mixture inhalation. The cardiac and respiratory systems are not depressed. The objection to paraldehyde is its all-pervading odour, but of this the patient, at any rate, seldom complains.

Intra-tracheal or endo-tracheal anæsthesia, first introduced into this country by Kelly, is now being extensively practised. The use of oxygen in the place of the hand-bellows and air-pump, and the improvements in technique have greatly added to its efficiency. The problem of the air-way, particularly in pharyngeal work, now becomes a far less formidable difficulty. It is frequently used, apart from any special necessity of the operation, when quiet respiration and minimum after-effects are desired. In head and neck operations, when compression or traction of the trachea may occur, or when blood or fluid are present in the pharynx, it is essentially the method of choice. By means of a second tube or catheter for expiration, and gauze packing, complete protection of the air-way is assured. The intubation of the larynx is a matter of practice, but it is very essential that the patient should be well anæsthetized and the pharyngeal reflex abolished before the catheter is introduced, and care must be taken not to injure the teeth, lips or tongue. Spraying with cocaine, and the stimulation of respiration with CO_2, are of assistance in cases of difficulty. Nasal intubation is sometimes preferable, especially for operations on the tongue or jaw. The relaxation and quiet breathing obtained by this method are always equal to, and frequently better than, that obtained in other methods of inhalation. There is no greater risk from bronchitis when ether is given in this way, and provided that gentleness is exercised in introducing the catheter, there should not be the least trauma to the vocal cords.

Perhaps in no way has the task of the anæsthetist been so much lightened as by use of "suction" in throat work. In those sometimes long and difficult dissections of tonsils, when hæmorrhage may be brisk and not easy to control, anæsthesia by the intra-tracheal method with a suction catheter in the pharynx or naso-pharynx makes all the difference. There are still surgeons who prefer to operate with anæsthesia maintained by chloroform, by means of a Junker inhaler, and who are adepts at controlling hæmorrhage without the use of suction; but when that skill is lacking, there is no doubt which method the anæsthetist prefers.

Local and regional anæsthesia has increased enormously in certain clinics on both sides of the Atlantic since the war. The increase has perhaps been greatest where the supply of skilled anæsthetists has been most deficient, and where the surgeons are disinclined to share the responsibility with an assistant. In England it has not been adopted to the extent that was expected, a fact which perhaps may be a credit to general anæsthesia, or, may be, the English temperament is not so well adapted to the idea of local anæsthesia or there is an established and ingrained hereditary preference for unconsciousness when being "cut about."

Spinal nerve-block by the injection of various drugs into the subarachnoid space is perhaps more used than ever before. There is no one method which can produce a combination of anæsthesia with such complete relaxation. The better understanding of the fall of blood pressure, the use of the "light" solutions, and the constant use of *some* degree of the Trendelenburg position, have practically eliminated subsequent headache. Prolonged paresis of certain nerve or skin areas has certainly followed spinal anæsthesia in a few cases, but invariably recovery has taken place. The various drugs are well known, but mention must be made of percaine, recently introduced; its advantages are low toxicity and very powerful action in an extremely dilute solution. Splanchnic nerve-block, by the injection of drugs into the tissues immediately surrounding the solar plexus, has been largely used in abdominal operations. When local anæsthesia or nerve-block is used, it is frequently in conjunction with some degree of basal narcosis, and possibly with gas-oxygen or other light inhalation. Opinion must vary as to the relative safety between local and general anæsthesia, and it must be remembered that by the very nature of their effects, the drugs used for local anæsthesia are powerful protoplasmic poisons. They may be given in a very diluted solution, but the total dose may not be inconsiderable, and the factor of idiosyncrasy must never be forgotten. A dose which may be safely injected into the tissues, may well prove fatal if inadvertently injected into a vein. That many fatal cases of bronchitis and pneumonia have occurred after local and regional anæsthesia must not be overlooked.

Some operations and procedures, for example, on the eye, nose, throat and bronchus, to mention only a few, can be carried out more easily and efficiently without loss of consciousness, in fact, in which consciousness may be desirable. The condition of the patient's heart or lungs may in some cases absolutely contra-indicate a general anæsthetic. The method is certainly inadvisable in children and young adults. Apart from such factors, the choice must always hinge on the temperament and mental condition of the patient, and whether or not he is likely to be the subject of psychical shock.

The education of students in anæsthesia has never been an easy matter, and to-day, with the multiplicity and complication of methods, it is more difficult. Even with the increase in operations the number of anæsthetics which any individual student can be permitted to give, even under supervision, is not nearly adequate to produce a trained and skilful anæsthetist. And it may be questioned if the average man now starting his career is as capable an anæsthetist as they were, say, twenty years ago. It may perhaps be said, even of anæsthetists, that they are "born and not bred," and it is very evident to those responsible for teaching students that many do not possess the desire, aptitude, nerve and temperament to become specialists. Every student, however, when qualifying, should be capable of giving an anæsthetic with ether, chloroform, or nitrous oxide. There must be many who have never seen, much less given, a pure chloroform anæsthesia. Yet there are surgeons to-day who demand chloroform anæsthesia, and while conceding the arguments against its use, when other and safer drugs are available, there are occasions and conditions when chloroform, and chloroform alone, can and must be administered. If students are taught to give chloroform-ether mixture on a lint mask, they will at any rate learn the principles of chloroform anæsthesia, and be less likely to be "found wanting" when the time comes.

ANÆSTHETICS IN GENERAL PRACTICE, WITH SPECIAL REFERENCE TO LOCAL ANALGESIA

By C. W. MORRIS, O.B.E., M.B., B.S.

Senior Honorary Anæsthetist, University College Hospital, London.

A CRITICISM once levelled at anæsthetics stated, with some bitterness and considerable truth, that they spared the patient only from the pain of the knife. Anyone who has been operated upon will readily agree that, great as that achievement is, it still leaves much to be desired. For instance, the apprehension beforehand, and the hours immediately following the operation, the actual discomfort of the absorption and elimination of the anæsthetic itself, are all features to be dreaded, and leave on the patient's mind a strong feeling of repulsion against further anæsthetics and operations. In the last few years considerable strides have been made, and the modern anæsthetist can do a great deal more than simply " blot out " the patient's consciousness during the time of the operation; and the criticism mentioned has been met to a great extent.

This improvement owes its achievement largely to two factors, first, the use of premedication before the anæsthetic is given, and secondly the increasing employment of nitrous oxide as the anæsthetizing agent. The object of the premedication is to put the patient into a condition as nearly resembling natural sleep as possible a short time before the anæsthetic is given and to keep the patient in this condition during the induction and for the first few hours after the completion of the operation. At the same time, the premedication will aid the anæsthetist in keeping the patient under with nitrous oxide, reinforced as necessary with a minimum of ether or chloroform.

To the practitioner who is called upon but rarely to give an anæsthetic the number of drugs used as a premedication, their action and mode of administration may be a little confusing, and the choice for any particular patient a matter of difficulty. Especially is this the case when he turns to some of the modern apparatus for giving gas and oxygen, with their complexity of taps, gauges, dials, safety-valves, and auxiliary feeds for ether, chloroform, and carbon dioxide. Unless he is prepared to spend some time in obtaining instruction and practice in mastering these machines he will be unable to get satisfactory results from their use. It is obviously impossible for every practitioner to afford the time or to have the opportunity for familiarizing himself with the action of all the modern preparations used as premedications, or to become proficient in handling many of the instruments now used for giving gas and oxygen combined with ether or chloroform.

There is, however, much that such a practitioner can do to give his patient some, at least, of the benefit of these improvements. In the first place, he can see that his patient has a good night preceding the operation, a point that is often overlooked, and which means a great deal to the patient. Medinal, gr. 7½ for an adult, will usually accomplish this, and not only prevents hours of sleepless worry but brings the patient to the operating table in a better condition to withstand the ordeal. Secondly he can use one or other of the premedications, and for this purpose nembutal will probably give the most satisfaction. This drug given by the mouth 45 minutes before the operation will prove in many cases a source of the greatest comfort to the patient. Two capsules, each capsule containing gr. 1½ of nembutal, are suggested as the dose to be given to an adult by the practitioner unfamiliar with the action of this drug. Even if sleep does not ensue in every case, the patient will be drowsy and benefit to the extent of being in a contented state of mind. Experience will enable the anæsthetist to judge the type of patient to whom he can safely give a larger dose, such as three capsules, or in rare cases four.

To allow the nembutal given in this manner to exercise its maximum effect it is essential that the patient be left perfectly quiet after swallowing the drug. All preparations must be completed and the hypodermic of atropine given beforehand so that the patient may be left undisturbed. In practice it is often difficult to get these rules observed, as some well-meaning person will insist upon disturbing the patient in an endeavour to make him more comfortable, or to have a talk before the operation. As the majority of patients are only lightly asleep under the drug and are easily aroused, any move from their bed or trolley to the operating room is liable to awaken them and defeat the whole aim of the premedication. To overcome this it is imperative that the induction of the anæsthetic should take place while the patient is lying in bed in his room. The anæsthetist should enter the room with the utmost quietness, and in favourable cases should find the patient asleep, usually curled up on his side. He should then without disturbing him, place over his face an ordinary open-ether mask on to the inner surface of which has been sprayed some 8 or 10 c.cm. of ethyl chloride. A few breaths of the ethyl chloride will be sufficient to keep the patient asleep, and ether can be added to the mask to complete the induction.

In this way it is possible for the patient to know nothing of the induction, and to remember only that he went to sleep in his bed and later woke up in bed to find the operation completed. In some cases the patient will merely be drowsy, and may speak when the anæsthetist comes in to start the induction, but the amnesia produced by nembutal is very striking, and he will in all probability have only a vague recollection of what took place. In houses where the transportation of an anæsthetized patient from his room to the theatre is difficult, it is wiser to place the patient on a bed or couch in a room convenient to the theatre before the nembutal is given, and to allow him to remain there till the induction is completed. Once the patient has been induced in the manner described and placed upon the operating table, the anæsthetic can be continued in any way that the anæsthetist may think best; gas and oxygen plus ether, or open ether, or chloroform can be used.

The induction of the patient who has had nembutal in this way is usually easy, but the anæsthetist must be on his guard against the patient being "asleep" and not properly under. The continuation of the anæsthetic calls for no special mention; gas and oxygen will be more readily taken and less ether required. A careful watch must be kept on these patients afterwards, as it is possible for them to get respiratory difficulties from swallowing the tongue or inhaling vomit. These complications are, however, extremely rare, for although the patient may be apparently sleeping for some hours after the operation, the protective reflexes of the pharynx and larynx return quickly after the withdrawal of the general anæsthetic. Operations upon the nose and throat can therefore safely be performed after nembutal has been given as described. Nembutal given by the mouth has been suggested as the premedication of choice on account of the ease with which it can be given, the pleasant way in which it can be taken by the patient, and the small amount of alteration from the established practice in the preparation of the patient for operation.

Nembutal given in this way shares certain disadvantages, which are common to all forms of premedication, whether given by the mouth, intravenously, or by the rectum. One is the occasional restlessness shown by the patient when coming round. This restlessness, when it occurs, varies from the merest turning from side to side in bed to violent and purposeless movements. The simple form, however, soon passes off, and is controlled by small doses of morphine. The violent type, fortunately rarely seen, may require, in addition to morphine, the presence of a nurse to restrain the patient's movements.

One other disadvantage of this method of premedication, again shared by most of the premedications, is the uncertainty of always inducing sleep. Two capsules of nembutal given by the mouth may produce sleep in an adult sufficiently deep to allow the patient to be carried down stairs on a stretcher to the theatre without waking, while at other times it may only produce a slight drowsiness. To attempt to overcome this difficulty some anæsthetists prefer to give two capsules the night before the operation, as a sleeping draught, and two more some 45 to 60 minutes before the operation. Others, again, give one large dose as a routine. Whatever method is used, its value will be greatly enhanced by rigidly observing the rule of keeping the patient absolutely undisturbed after taking the drug, and by carrying out the induction while the patient is still in bed.

Another precaution that can be taken by every anæsthetist, and one that adds to the comfort and safety of the patient, is the administration of a few breaths of carbon dioxide gas, preferably with oxygen, at the end of the operation. Carbon dioxide is now available in handy "sparklet" form, which makes it readily accessible to all anæsthetists. The thorough ventilation of the lungs produced by this powerful respiratory stimulus both washes out the anæsthetic and acts as a safeguard against pulmonary congestion. Patients after carbon dioxide come round more rapidly and regain more quickly their laryngeal reflexes.

LOCAL ANALGESIA

Turning from the subject of general anæsthesia to local analgesia, one feels perhaps that it is not so fully appreciated as it should be, considering its many advantages. For practitioners working single-handed in their own surgeries, faced with one or other of the many minor conditions requiring surgical aid, local analgesia affords the ideal solution of the anæsthetic problem. There are several drugs capable of producing local analgesia when injected into the tissues, and satisfactory and constant results can be obtained with novocain, pantocaine or novutox. Cocaine, even in weak solution, should never be injected on account of its highly toxic character. I am accustomed to use solutions of novocain of either ½ or 1 per cent., which make a useful medium for general work, and produce an analgesia lasting for at least an hour. These solutions are unaffected by boiling and can be kept for long periods without losing their properties. Large quantities up to 4 or 5 oz. can be safely injected into the body without fear of toxic results. The only apparatus necessary is a good syringe and a set of sharp needles, varying from fine hypodermics to those of from two to three inches long. Needles capable of bending are the safest as they are less likely to snap off when being used.

For infiltrating small areas a hypodermic syringe will meet all requirements. "Continuous flow" syringes, in which it is unnecessary to disconnect for each refill, can be obtained, and save time and labour when extensive infiltrations are carried out. The addition of adrenaline, one in 1,000, in the proportion of 2 drops to each fluid ounce of novocain solution will constrict the vessels and so reduce hæmorrhage in the infiltrated area, and will retain the solution in that area, thus producing a longer period of analgesia.

Aseptic precautions must be observed for all infiltrations and nerve blocks, undertaken for producing local analgesia, and the patient's skin, the anæsthetist's hands and instruments must be prepared as carefully as they are for major operations. The novocain must be made up in a sterile solution. For the type of cases under consideration simple infiltration—analgesia will be found most useful—nerve blocking alone is more difficult to carry out, and unless it is done successfully, a patchy unsatisfactory analgesia will be the result. In practice it is often convenient to combine the two methods. For small operations a line of infiltration along the proposed incision will be all that is required. To effect this so that the patient may feel as little discomfort as possible, a small bleb is raised in the thickness of the skin at one end of the proposed line, by injecting a few minims of the novocain solution through the finest hypodermic needle. Through this bleb can be thrust a needle of greater calibre and length, and the infiltration can be continued under the skin along the required line. While the needle is thrust slowly forward to its full reach beneath the skin, the plunger is gradually pressed home, the area of infiltration becoming visible as the solution spreads in the subcutaneous tissues. Further insertions of the needle are made through the area already injected and the required region rendered analgesic with the minimum of pain to the patient.

Care must be taken when infiltrating in the neighbourhood of vessels to see that the needle does not enter their lumen; toxic results may follow the injection of novocain directly into the circulation. By withdrawing the plunger and noting whether blood is sucked up into the syringe it is possible to make sure whether the needle is free of the vessel.

For removal of lipomas, adenomas, sebaceous cysts to mention but a few of the conditions likely to be met with, when it is not practicable to remove them through a linear incision an elliptical area of infiltration should be laid down round the proposed field of operation. Care also should be taken to inject beneath the tumours. The secret for assuring a painless operation is to use a large quantity of the solution, and infiltrate widely and thoroughly.

It is unnecessary to enumerate the occasions in which the production of analgesia in this way, or some modification of it, will prove useful and save the patient from the unpleasantness of a general anæsthetic. For operations upon a finger or toe, for removal of a nail or exostosis, opening a whitlow, sewing up a cut, or extracting a foreign body, etc., the procedure is a little different. In this case, a ring of novocain solution is injected round the root of the digit, under the skin. If adrenaline is added it must be in very small quantities, otherwise a profound ischæmia may result, interfering with the healing of the wound. One puncture with a hypodermic needle on the dorsum of the finger will allow both sides to be infiltrated, and one more insertion should enable the anæsthetist to complete the ring. Analgesia spreads slowly towards the tip of the finger, and it is necessary to wait some minutes before the whole finger becomes anæsthetized. It is undesirable to infiltrate into an area which is septic, and unless that area can be rendered analgesic by blocking the sensory nerve or nerves supplying it at some distance from the sepsis local analgesia should not be used.

In performing major operations under local analgesia we are faced with rather a different problem, as the patient's reaction becomes more important. Most patients are willing and often only too anxious to avoid a general anæsthetic for a minor operation, but comparatively few are prepared to face the ordeal of a long operation under local analgesia. Some, however, will go to any length to avoid a general anæsthetic, and these with their whole-hearted co-operation with the anæsthetist prove the ideal patient for this type of work. It must be remembered that in a successful local analgesia freedom from pain can be obtained, but some tactile sensations remain and some discomfort may be felt by the patient from dragging, transmitted from the analgesic to the sensitive parts. These sensations coupled with fright and expectation of being hurt produce a state of shock detrimental to many patients.

Operations carried out on a fully conscious patient also impose irksome restrictions on the surgeon. It is here again that premedication proves of great assistance. Nembutal given as already described may keep the patient calm and help him over the trying period of the operation, but as a rule a drug acting with greater potency than nembutal by the mouth is required. A full dose of morphine given beforehand may prove sufficient, or else avertin per rectum will produce the desired effect. A local infiltration, or nerve blocking, combined with gas and oxygen anæsthesia with or without ether, following a premedication with nembutal, will provide the pleasantest form of anæsthetic for many operations, and will spare the patient the alternative heavy dosing with ether.

There are types of cases in which local analgesia is specially called for. These include patients requiring a tracheotomy, gastrostomy or an empyema drainage, and may be briefly referred to. Such patients are frequently in a condition that renders a general anæsthetic highly undesirable, and in all cases the operation can be satisfactorily performed under local anæsthesia. In the case of the tracheotomy a subcutaneous line of infiltration is laid down in the middle line from the cricoid cartilage to the manubrium sterni. Before opening the trachea one c.cm. of 10 per cent.

cocaine solution should be injected into its lumen by means of a hypodermic needle: this helps to check the paroxysms of coughing which otherwise would ensue when the tracheotomy tube is first introduced.

For the performance of a gastrostomy the operation may be carried out either under local infiltration or by blocking the intercostal nerves. The former is the more easily achieved. The subcutaneous band of infiltration is made along the left rectus muscle extending from just above the costal margin to the umbilicus. Deeper infiltration is then made into the rectus sheath and muscle, and deeper again to endeavour to inject the peritoneum lying below. This is repeated till the whole line to the umbilicus is deeply infiltrated. Should the patient complain of pain during the operation when the peritoneum is exposed, this can be rendered analgesic by direct infiltration. The solution should be used freely and four or five ounces of ½ per cent. novocain with adrenaline can safely be injected. The opening of the stomach does not disturb the patient, provided no traction is made.

The resection of a part of a rib for draining an empyema can be carried out under local analgesia without difficulty. The exact portion of rib for removal is first determined, and a line of subcutaneous novocain placed along the proposed incision. The needle is then thrust down to the rib at the dorsal limit of the section for removal, and its lower edge felt. The point of the needle is then directed up into the subcostal groove and 5 c.cm. of novocain injected to block the intercostal nerve. The point of the needle is then brought into contact with the outer surface of the rib, and the periosteum infiltrated over the length of the part to be removed. The intercostal space immediately above and below the selected portion of the rib is then thoroughly injected and the two intercostal nerves blocked in a similar way.

THE PROGRESS OF ANÆSTHESIA

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THE advances in surgery have been made possible by those in other branches of science, particularly chemistry and biology. Anæsthesia and asepsis were the logical outcome of the application to surgery of discoveries in these sciences. Given anæsthesia and asepsis, surgeons have been enabled to develop operative technique to the extraordinary degree of perfection which now exists. It is surprising that this period of development in surgery has not been accompanied by any comparable development in the field of anæsthetics until comparatively recent times.

If statistics were available for all anæsthetics given in the British Isles at the present time, it is probable that administrations of chloroform or ether by a simple method would occupy a dominant position. It is true that many operations of a serious nature are performed under this type of anæsthesia with complete satisfaction to all concerned. When time, expense, or expediency demand first consideration, simple methods will continue to have their place, and in the teaching of students, simple methods offer the best basis for fundamental observation.

Ether and chloroform continue to be used because of the reliability of the anæsthesia which they produce and the ease and simplicity with which they can be administered in the average case. This, however, should not be allowed to obscure the fact that both substances are protoplasmic poisons producing destructive changes in all living cells. This toxic effect may easily turn the scales against a patient whose general resistance is already weakened by disease.

Ether and chloroform do nothing to save the patient from unpleasant anticipation and apprehension before the operation. Induction with either of them is unpleasant to most people, and the recovery period, with its attendant nausea, is one which few are anxious to experience again. Many will regard this picture of the situation with reference to the average case as overdrawn. The fact remains that patients frequently dread the anæsthetic more than the operation itself. This is particularly true of the patient who has had previous experience of a so-called "straight" anæsthetic. Research in anæsthetics has, however, been productive of practical results in two directions: (1) The introduction of improved methods of administration. (2) The discovery of a number of agents which enable the anæsthetist to dispense with chloroform and ether in many operations and to limit their employment to a minimum in others.

IMPROVED METHODS OF ADMINISTRATION

The chief development in methods of administration has been consequent upon a closer appreciation of certain elementary physiological facts. It has long been recognized that a free air-way is essential for safe and satisfactory anæsthesia. Partial obstruction of the air-way gives rise to a syndrome fraught with both difficulty and danger. The signs are only too familiar: laboured respiration, congestion, increased secretion of mucus—itself a further cause of obstruction, cyanosis. The succession of events constitutes in itself a vicious circle. It is highly probable that many deaths ascribed to the anæsthetic agent have been due primarily to obstruction of the air-way.

A minor degree of respiratory obstruction may be of little or no consequence when the operation is of short duration and the patient is in reasonably good condition; but in operations of a prolonged and serious nature and where the patient is a bad operative risk, the slightest extra burden on the mechanism of respiration and circulation reacts to his detriment. Minor degrees of respiratory obstruction have been dealt with in the past by well-known simple methods, such as altering the position of the head, supporting the jaw, or the use of a pharyngeal air-way. Such measures may suffice in many cases, but frequently they are inadequate.

Intubation is the solution of the problem of respiratory obstruction and is the basis of what is now known as endo-tracheal anæsthesia. Type of patient or nature of operation may often justify anticipation of respiratory obstruction. In such cases it is easier and safer to intubate before the signs appear, for prevention is better than cure, whatever the dramatic superiority of the latter. The mere mention of endo-tracheal anæsthesia is liable to conjure up a vision of complicated and cumbersome apparatus. Special apparatus providing for more accurate regulation of the supply of the anæsthetic is always useful. Where positive pulmonary ventilation is required apparatus is essential; but in all other cases the provision of an air-way that is proof against obstruction is the basic feature involved. It is highly desirable that all who may be called upon to administer an anæsthetic should become proficient in simple intubation. Once an anæsthetist has acquired the technique he will find himself relieved of most of the difficulties which may beset him in the operating theatre. When the site of operation is the head or neck he will no longer find himself involved in continual strife with the surgeon for the maintenance of the patient's air-way; when he has a short-necked, fat person undergoing cholecystectomy he will find himself able to secure muscular relaxation without needing to "saturate" his patient to the last degree, for once laryngeal obstruction has been rendered impossible, the amount of anæsthetic required is considerably reduced. This reduction in the amount of the anæsthetic required and the absence of congestion diminish the tendency to post-anæsthetic toxæmia and pulmonary complications. Intubation in itself is an undoubted advance, even though the anæsthetist may feel constrained to adhere to his use of the mask and drop bottle.

Technique of intubation.—The technique of intubation is easy to master. The only equipment necessary is a laryngoscope (which should be at hand in every modern operating theatre), and a range of suitable rubber tubes. Rubber tubes for the purpose are now manufactured in a series of twelve sizes from $\frac{8}{64}''$ to $\frac{3}{8}''$ calibre. The ends are bevelled and smoothed to facilitate introduction. Preliminary spraying of the larynx with a small quantity of 20 per cent. cocaine solution from a nebulizer renders deep initial anæsthesia unnecessary.[1] The patient's head should be placed in a natural position; it should be neither fixed nor extended. When intubating through the mouth the easiest method is to use the laryngoscope, but the writer's "blind" technique[2] is so simple that it is always worth while exploring the possibilities of the nasal route when there is a free choice and when no contra-indication, such as sinus infection or gross nasal deformity, is present. The chief complication of intubation is post-anæsthetic sore throat. This is usually transient and occurs in only a small percentage of cases. The cause is undoubtedly trauma. It can, therefore, be avoided by careful technique.

Precautions (in intubation).—It should be borne in mind that preliminary medication dries the mucous membranes of the upper air passages. The dryness is aggravated by induction of anæsthesia with nitrous oxide from which all moisture has been removed. To counteract the obvious liability to instrumental trauma of mucous membranes in this condition, a gargle containing glycerin should be used before anæsthesia is induced. Children may be given a few drops of glycerin in water to swallow. Gaseous anæsthetics should always be moistened before they reach the patient. The endo-tracheal tube and the blade of the speculum should be sterilized and thoroughly lubricated with vaseline. Intubation interferes with the protective reflexes of the larynx. It is incumbent on the anæsthetist, therefore, to safeguard the patient against the entry of blood or vomitus into the trachea through the space between the vocal cords and the endo-tracheal tube. It is during inspiration that this is most liable to occur. Protection is effected by carefully packing the pharynx with a muslin bandage previously boiled in vaseline. In intestinal obstruction associated with fæcal vomiting the method is unsafe in this respect unless used in conjunction with positive endo-tracheal pressure or the simultaneous introduction of an œsophageal tube.

Contra-indications (to intubation).—Notwithstanding the numerous advantages of intubation in anæsthesia there are some operations in which it is contra-indicated: (1) In operations upon the eyeball the slightest cough during operation and any tendency to post-operative vomiting must be prevented. (2) In operations for the removal of fungating growths in the hypo-pharynx and the neighbourhood of the superior opening of the larynx there is a risk of dislodging pieces of growth into the trachea during intubation. (3) In goitre operations intubation would involve a deeper induction and maintenance level than is either necessary or justifiable. Exception is made in those cases in which the pressure upon the trachea is likely to cause a prolonged and otherwise uncontrollable state of asphyxia during the operation.

The rôle of carbon dioxide.—No account of methods of administration can be considered up-to-date without some reference to the uses of carbon dioxide, which is at once a weapon of offence and defence and as such is a valuable addition to the armamentarium of the anæsthetist. It can be used with advantage to hasten induction or deepen anæsthesia when respiration is lagging. It stimulates abduction of the vocal cords and facilitates intubation. At the end of an operation it promotes activity in the pulmonary circulation and helps to prevent pneumonia. It may be used to expedite the restoration of consciousness when this is desired.

Substitutes for ether and chloroform.—So far as general anæsthesia is concerned, no substance has yet been discovered which, when given by itself in comparatively safe doses, can be as efficient as ether or chloroform. Investigations, however, of these different agents have brought to light the peculiar advantages and limitations of each. The idea aimed at in their use is to balance the anæsthetic, like a prescription or diet, by careful selection.

Nitrous oxide in combination with oxygen occupies a place by itself. The combination is non-toxic, and for this reason alone would be the anæsthetic of choice in every case where a general anæsthetic is required; but unfortunately it does not produce muscular relaxation sufficient for many operative procedures. Considerable pre-operative medication, as by one of the basal hypnotics, or in combination with local anæsthesia are necessary if nitrous oxide and oxygen are to supply the operating conditions demanded for abdominal surgery. For example, in the surgery of the upper abdomen, the attainment of muscular relaxation with nitrous oxide and oxygen involves a degree of suboxygenation more harmful to the patient than the addition of the necessary amount of ether.

Ethylene and oxygen produce a much more satisfactory anæsthesia than nitrous oxide and oxygen. A greater degree of muscular relaxation can be obtained without necessity for sub-oxygenation. Unfortunately the smell of ethylene is annoying, and its use also involves the possibility of explosion. For these reasons ethylene remains unpopular in this country, which is to be regretted as it possesses such definite advantages. Ethylene is widely used in America and Australia, although the possibility of explosion from static electricity is much greater there than it is in Great Britain. When it becomes generally realized that the explosion risk with ethylene is in reality no greater than with mixtures of ether and oxygen already in common use, it is likely that ethylene will attain the popularity it deserves.

BASAL HYPNOSIS

It is imperative in the first place to discriminate as accurately as possible between true basal hypnosis and what is called in America "pre-operative sedation." Sedation with morphine or morphine and scopolamine, or with a small dose of one of the barbiturates is a recognized procedure. With this form of medication there is not any guarantee that the patient will be unconscious before the anæsthetic is administered. In true basal hypnosis, on the other hand, complete amnesia is effected before induction of anæsthesia, and failure in this respect may be interpreted by the patient as incompetence on the part of the anæsthetist.

The advantages of basal hypnosis are well known. The patient passes quietly into a state of amnesia or sleep while still in bed. It is frequently possible for the operation to be performed under nitrous oxide and oxygen without any cyanosis. When ether is necessary for muscular relaxation the quantity required is minimal. In many cases only local anæsthesia is required to supplement the basal hypnosis. A period of amnesia follows the operation and nausea is slight or absent. In fact, successful basal hypnosis may be proved to be the groundwork of an ideal.

Precautions.—When the anæsthetist undertakes to place a patient in a state of basal hypnosis before an operation, caution is essential if the desired state is to be arrived at with accuracy and safety. It must be borne in mind that the response to a given drug, and particularly to a hypnotic, may vary considerably with the individual. The calculation of the dose on a body weight or age basis is, therefore, at best a mere approximation to the correct dose in a given case. Accurate dosage can only be arrived at in the human being by judging the response during the course of administration. For this reason the responsibility of the anæsthetist is no whit less when the patient is in bed than when he is on the operating table. It is desirable to lay stress on this point, for it is no uncommon practice to relegate the administration of the basal hypnotic to any nurse when the rectal route of administration is chosen.

Before giving a basal hypnotic it is advisable to be certain that both drug and procedure are approved and understood by all concerned in the operation. The care of the patient during the immediate post-operative period should be explained, particularly to the nurse. It is of supreme importance at this time to withhold the administration of any further hypnotic or opiate until consciousness is recovered. All basal hypnotics have a depressant action on respiration. If the dose has been correctly judged the depression in respiration is no greater than in normal deep sleep. Should respiration become so shallow or so decreased in frequency as to be accompanied by cyanosis in spite of a free air-way, overdose is the only description applicable to the condition. Finally, it is well to realize that basal hypnosis is no panacea for a badly administered supplementary anæsthetic.

Disadvantages of basal hypnosis.—The chief disadvantage is the necessity for accurate regulation of the dose. The responsibility for this essential part of the procedure throws an additional burden on the anæsthetist, but the gratitude of the patient does much to reward him for the extra trouble entailed. It is commonly asserted that basal hypnosis throws much extra work upon nurses. If the foregoing precautions regarding the regulation of the dose are observed, the special nursing attention required by the patient in the immediate post-operative period need be no greater than that to which he is entitled after open ether. Restlessness occurs occasionally during the period of recovery, but this is not always absent in recovery from unconsciousness however produced. In any case, the incidence of restlessness is sufficiently infrequent for its import to be negligible in view of the general advantages of the method.

Drugs for basal hypnosis.—Probably the most valuable drugs available for basal hypnosis at the present time are: (1) paraldehyde, (2) avertin, (3) certain derivatives of barbituric acid.

(1) *Paraldehyde* is a well-known drug with a wide margin of safety. Its use is rarely followed by restlessness. For these reasons it is particularly suitable for young children. The employment of paraldehyde per rectum as a true basal hypnotic was established by Rowbotham in the year 1923. In the doses recommended by him of one drachm per stone body weight in 10 per cent. saline (with due allowance for the condition of the patient), satisfactory basal hypnosis can be obtained in average cases. As with all basal hypnotics the administration is important since it is not uncommon for the patient to reach the desired

state before the full injection has been given. Paraldehyde has waned in popularity chiefly because of its objectionable smell and not on account of any inherent inefficiency.

(2) *Avertin* is perhaps the most popular basal hypnotic at present in use. Its value is undisputed. The peculiar virtue of avertin lies in its possession of considerable anæsthetic properties even when given in safe doses. Its capability of inducing muscular relaxation makes it the agent of choice in abdominal operations when there is no contra-indication to rectal injection. It must be remembered that general muscular relaxation is often accompanied by a tendency towards obstruction of the air-way. A constant watch for this must be maintained. Avertin is a most powerful drug and the greatest care should be exercised in regulating the dose. A most satisfactory procedure is to measure out the dose on a basis of 0·1 gram per kilo. body weight and to give half the solution half-an-hour before the appointed time of operation. After an interval of ten minutes the response of the patient is observed and further portions of the calculated dose are given at short intervals. By proceeding in this fashion it will often be found unnecessary to give the whole of the calculated dose. In any case such fractional administration widens the margin of safety.

(3) *Nembutal* (pento-barbital sodium) is probably the most valuable derivative of barbituric acid for basal hypnosis in anæsthesia. It can be given by mouth or by rectum, but it is difficult to obtain accurate results by either of these routes. The virtue of nembutal is the fact that it can be given intravenously. The most satisfactory effect is obtained when the administration is preceded by a hypodermic injection of omnopon gr. 1/3 and scopolamine gr. 1/150 one hour previously. The subsequent dose of nembutal required is consequently small. The combination

with omnopon and scopolamine is important. Restlessness is liable to occur during detoxication of the drug, as with all barbiturates, and the smaller the dose the less is the risk of this complication. The intravenous injection should not exceed 1 c.cm. per minute. The correct dose is estimated by the effect obtained during administration in the same manner as with a volatile anæsthetic. When marked drowsiness supervenes the injection should be stopped. This usually happens after gr. 3 to gr. 6 have been given. Although larger doses (up to gr. 7½) may be safely given, the injection being continued until the patient no longer responds to questions, experience shows that nothing is to be gained by such a procedure. Nembutal in basal hypnotic doses is purely amnesic. In contrast to avertin, nembutal in these doses possesses in itself scarcely any anæsthetic qualities, nor does it produce muscular relaxation. Willcox[3] reports that nembutal has a destructive action on the kidney. No doubt this may be observed when an overdose has been given. In my experience of more than 1,500 cases of intravenous nembutal injection these deleterious results have not been observed.

LOCAL, REGIONAL, AND SPINAL ANALGESIA

While the majority of British surgeons have remained content with the doubtful perfection of ether " saturation," research on the Continent has been directed towards the development of local and regional analgesia. It is not improbable that this trend abroad has been due to some extent to a dearth of competent administration of general anæsthetics. The perfection attained in local and regional anæsthesia is already such that practically any operation can be performed upon a fully conscious patient without inflicting actual pain. Spinal analgesia may now be regarded as a branch of regional anæsthesia and has been perfected to an equal degree as far as the provision of good operating conditions is concerned. However excellent the anæsthesia obtainable by these methods, they give very little consideration to the psychic trauma they produce.

The combination of basal hypnosis with either of these methods would seem at first an ideal proposition. It is certainly practical in selected cases. In the more extensive sphere of splanchnic analgesia or high spinal analgesia for upper abdominal surgery a considerable fall in blood pressure is frequently encountered; it would appear inadvisable to add to this the depressant effects of a basal hypnotic, particularly in bad-risk cases.

THE FUTURE OF ANÆSTHETICS

From this brief account of the developments in anæsthetics it will be apparent that there is a tendency to depart from the simple methods of the past. Is this justifiable? Atraumatic anæsthesia is the ideal to be attained. If this be granted, it is logically indefensible to subject the whole organism to profound narcosis in order to secure anæsthesia in one particular region when the necessary conditions are obtainable by methods which are less injurious, even though they may be more complicated.

A comparison between British and Continental practice in anæsthetics indicates a possible route to the attainment of improved operative results. In Great Britain, owing to the relatively high standard of administration, general anæsthesia still holds the field for the majority of operations, whereas the trend on the Continent has been towards perfection in regional methods. Abdominal surgery is perhaps the severest test of the effects, both immediate and post-operative, of an anæsthetic. It is in this field particularly that regional methods have proved so successful. Finsterer has demonstrated the superiority of his operative results obtained by this method over those obtainable with any form of general anæsthesia. It is unlikely, however, that regional anæsthesia *per se* will become popular in this country. The average British patient demands general anæsthesia for major operations; in future he is likely to demand absolution, within reason, from undesirable effects associated with the administration. Experience shows that the combination of careful basal hypnosis with innocuous agents such as nitrous oxide and oxygen is an improvement in this direction. In the fulfilment of the immediate needs of the surgeon for muscular relaxation, a synthesis of British and Continental practice seems to be indicated. As the welfare of the patient is the common aim of both surgeon and anæsthetist it must be admitted that muscular relaxation obtained by limited field-block of the abdominal wall is just as satisfactory as that which follows the use of ether and avoids the after effects of the latter.

The pursuit of the ideal requires earnest co-operation between surgeon and anæsthetist; it entails more trouble for both. In the supervision of basal hypnosis and the administration of nitrous oxide and oxygen the anæsthetist is fully occupied at the time when the local infiltration is required—that is, when the patient is on the table. The necessarily aseptic infiltration can be carried out by the surgeon or a competent assistant before the incision is made. It is not improbable that in the future combined anæsthesia of this type will, when practicable, become a recognized technique. Once it is established it is reasonable to expect not only a reduction in operative mortality but a shorter and more comfortable convalescence.

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SOME PRACTICAL POINTS APPLICABLE TO ANÆSTHESIA IN CHILDREN

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THAT the study of anæsthesia in children is just as much a special branch of anæsthesia in general as pediatrics is of general medicine, is now an acknowledged truism. This is so because of the relatively more delicate frame and structure of the child in comparison with those of the adult. The subject may be considered separately from two aspects, the psychological and the physical.

There is an almost endless amount to be said about the former point of view. In the distant past the nervous system of numberless children must have received irrevocable damage from the failure to realize, or at any rate to combat, the amount of mental shock which the clumsy or forcible induction of anæsthesia could cause a child, and more particularly a "nervy" child. It is essential for the peace of mind of the child that the induction should be approached with considerable care and tact, and the ways and means of rendering the inductions free from fright, or even unpleasantness, should be carefully considered. Every child is apprehensive about a fresh face, and almost invariably the anæsthetist is a stranger to the child who is to have the operation. So our efforts should be directed towards some means whereby the terror a child may suffer on being approached by a strange doctor, with a face-mask and other paraphernalia, may be completely prevented.

For many years those particularly interested in this subject have been working with the above object in view. Numerous medicaments have been tried, and until recent years nothing both safe and effective had been found. Morphine and heroin were used, but, owing to the action of both these drugs on the respiratory centre, respiration became slow and shallow, and therefore complete anæsthesia with ether was difficult or impossible to induce, and complete relaxation was not obtainable. Children are peculiarly bad subjects for morphine and its derivatives, and to administer them was found to be unsafe. Cessation of respiration was frequent, and so the use of these opiates had to be discontinued. Hedonal, urethane, and alcohol were all tried, but proved dangerous and impracticable. No preparation of bromide was found to be efficient. Furthermore, intravenous injection as a premedication is almost as alarming an adventure for a child as a direct inhalation.

The goal aimed at has been a form of premedication which can be administered easily without alarming the child, induces sleep gradually and without discomfort, and is completely safe. The essential qualities for safety are: (1) no depressing action on respiration; (2) no depressing action on the heart; (3) does not reduce blood pressure; (4) does not act on the kidneys; and (5) is easily eliminated without injury to the tissues.

No drug which does not fulfil all these conditions can be considered permissible for premedication of the child, for each requirement is equally important. In recent years several preparations have been put upon the market claiming to possess one or more of the above essentials, and some of them have proved of great service in the premedication of adults. But none has possessed all the essentials combined. The delicate nature of the tissues of the child, with the margin for error so minute, and the knowledge that the child reacts so rapidly, or perhaps alarmingly suddenly, as to bring him into the danger zone without warning, makes it imperative that an anæsthetic should not be administered to a child after the premedication of any preparation which does not entirely possess all the essentials enumerated above. Fortunately there is one drug which does fulfil all the necessary qualifications for the premedication of a child after which it is absolutely safe to administer deep anæsthesia, and that drug is paraldehyde.

Paraldehyde ($C_6 H_{12} O_3$) is prepared by the actions of hydrochloric or sulphuric acid on aldehyde; during the action the mixture becomes hot and, on cooling to 32° F., paraldehyde crystallizes. At a temperature above freezing point paraldehyde is a colourless liquid; it is soluble 1 in 10 in water; it is not soluble in oil. It is a powerful hypnotic without any unpleasant after-effects; it acts quickly, it somewhat strengthens the heart, does not have any effect on the respiration, and does not affect the gastro-intestinal tract; it is a mild diuretic. It is largely excreted by the lungs, and therefore the breath smells strongly of the substance until elimination is completed; it has an unpleasant odour, but the patient is unaware that the breath smells unpleasantly. It should be kept in a cool, dark place, otherwise it may disintegrate and glacial acetic acid be formed.

Paraldehyde has a most unpleasant taste and therefore cannot be given to a child by the mouth; it should be injected per rectum, being dissolved in normal saline, the proportion of one part of paraldehyde added to eleven times the amount of saline, a solution of 1 in 12—i.e. 1 drachm of paraldehyde up to 1½ ounces of normal saline. It should never be given in oil, as it only floats on the oil or forms an emulsion, with the consequence that it is irregularly absorbed, and causes severe irritation of the rectal wall at those points where it is in direct contact with the mucous membrane.

The dosage has the advantage of simplicity, and it is given according to the body weight of the child, 1 drachm to each stone of body weight. It is important that the dose should be regulated in this way, and not by age. Thus, for a child weighing 3½ stone, 3½ drachms of paraldehyde should be put into an 8-oz. bottle and saline added up to 5 oz. and 2 drachms. This will leave ample room in the bottle for the fluid to be shaken up and so insure a perfect mixture. The bottle should be stood in warm water so that the fluid is warmed, the requisite temperature being about 92–94° F. This should be introduced into the rectum by means of a catheter, tube or funnel, and it is important that the fluid should be slowly run in, taking about a quarter of an hour to twenty minutes in the act. The child can easily be persuaded not to expel the fluid, and so long as it is only run in slowly it is not resented by the child, but any attempt at haste the child will resent, and there is a likelihood that some of the fluid may be returned. This procedure is carried out by a trained nurse who only needs to possess average tact and, of course, gentleness, to insure success.

It is advisable that the rectum should be empty so that the paraldehyde is retained, and with this object the operation should be arranged at such a time as to allow the child to have his ordinary motion in the morning, play about as usual after a normal breakfast, and receive the paraldehyde at noon or soon afterwards. He will be asleep within forty minutes and will not resent a hypodermic of atropine an hour after the beginning of the introduction of the paraldehyde. It has been found that the ideal plan is, paraldehyde begun at noon, hypodermic of atropine at 1 o'clock, and operation at 2 o'clock.

The induction of anæsthesia is carried out with the child in his cot. He is sound asleep, with the retention of all his reflexes. Just as a child may be seen to brush away with his hand a fly that has settled on his face during sleep, so will he tend to raise his hand and push away the face-piece if it touches his face during the early stage of induction. So care must be exercised not to touch the child, particularly the face, until anæsthesia has advanced. Ether is irritating and may cause much movement, and so induction must be effected by some less pungent anæsthetic. The ideal anæsthetic for this purpose is ethyl-chloride with eau-de-Cologne, and Messrs. Duncan and Flockhart have prepared this combination in a conveniently shaped bottle admirable for the purpose. A little should be sprayed on to the gauze (in any of the ordinary face-pieces) and the child allowed to inhale this for a few breaths, until the buccal mucous membrane is anæsthetized, when more of the ethyl-chloride may be sprayed on to the gauze and the face-piece placed nearer to the mouth. After about twenty breaths the anæsthesia will be such as to allow the face-piece to be adjusted on to the face, more ethyl-chloride again added and anæsthesia pushed a stage further. After this the child may be placed on his back and ether substituted for the ethyl-chloride, the administration of anæsthesia being continued in the ordinary way. It is then perfectly safe to carry the child from his cot to the adjacent operating-room, when the usual routine is proceeded with. After the operation the child will be carried back to his cot and will continue to sleep soundly and peacefully.

The hypodermic injection of atropine sulphate is, of course, a necessity, and the following table of dosage is carried out by the writer :—

From birth to 6 months	1/400 grain
From 6 months to 1 year	1/200 grain
From 1 year to 2 years	1/150 grain
Over 2 years	1/100 grain

Having been in his own cot when the paraldehyde was introduced he will have known nothing about the events to come, and when he awakens several hours later, still in his own cot, the operation is over, he has not been conscious of any active interference or strangers in his room, and so there has been no upset to his nervous system. There will be no question of mental terror at the future visits of the doctor, and this will be found of inestimable value to the parents as well as to the child. In fact, he has no knowledge that he has had an anæsthetic. The child is likely to sleep after the operation for six to twelve hours, and when he awakens he will be able to have a drink and probably have a conversation with those near him before going to sleep again for another spell of from six to eight hours. On the following day he will be quite oblivious to the conversation which he had during the time when he had been awake.

Reference has been made above to the induction of anæsthesia in children by ethyl-chloride and eau-de-Cologne, a most valuable preparation which it may be useful further to describe in this article. It has been stated that ethyl-chloride is a dangerous anæsthetic, and I am anxious to emphasize that such is certainly *not* found to be the case after a personal experience of over sixty thousand such inductions in children without one moment of anxiety. The primary essential in the administration of anæsthesia is a free air-way; important as this is in all cases its importance cannot be too strongly stressed when the patient is a child, whose balance can be so easily disturbed with such disastrous consequences by even a few seconds of cyanosis. When cyanosis occurs, the right side of the heart dilates, and consequently the child is immediately placed in the danger zone. Even if the cyanotic state is only momentary, sufficient damage has been done to that small heart to jeopardize the child's life while an operative procedure is taking place so soon afterwards. The difficulties that may be encountered in the induction of anæsthesia by ethyl-chloride may be centred on the contractions of the muscles attached to the jaw which is caused by ethyl-chloride. In the course of the onset of anæsthesia the first stage commences after four or five breaths, but it is only fleeting if the face-piece is removed; when ethyl-chloride inhalation continues, the second stage is reached and is characterized by two definite phenomena: (1) tonic contraction of the masseter muscles; (2) temporary respiratory inhibition. These are synchronous and pass off completely. Respiration is only inhibited for a very few seconds, and, as soon as it restarts, the further inhalation of the ethyl-chloride causes the masseters to relax and anæsthesia to continue to the third stage, that of complete analgesia, and then the face-piece can be removed and a minor operation be performed—or ether may be dropped on to the gauze and prolonged ether anæsthesia be obtained.

It is to be noted that during the second stage the jaw is fixed by the contraction of the masseter muscles and therefore it is of vast importance that the mandible should be in such position that when the contracted muscles cause this fixation the air-way should be patent. It is at this stage that there is a fleeting period of cessation of respiration, and, as soon as the respiratory mechanism restarts, a free air-way is essential.

If the air-way is not patent while the masseters are in a condition of spasm the difficulty of repositioning the jaw is insuperable, and it is necessary to wait until the spasm has passed off, when the mandible can be readjusted. To struggle with the jaw at this particular stage will only tend to throw the head forward and constrict the trachea and larynx, thus further obstructing the air-way. In this manner only can cyanosis be avoided. But it is really a very simple matter so long as the essential maxim be observed, "Keep a free air-way." When this difficulty is encountered and cyanosis occurs, it has been brought on either by the anæsthetist's sins of omission in not preserving a free air-way, or sins of commission in struggling with the jaw while the masseters are in a condition of tonic contraction, but is not primarily caused by the anæsthetic.

Ethyl-chloride, when combined with eau-de-Cologne and used at first in small quantity, does not irritate the upper air-way, and is the ideal anæsthetic for induction in children. With ether, in sequence, a complete anæsthesia is easily obtained, and is in no way contra-indicated. For dental cases it is far superior to nitrous oxide. The ordinary metal frame covered with gauze is not nearly so alarming to the child as the rubber face-piece and cumbersome bag of the nitrous oxide apparatus. The face-piece should be held well away from the mouth at first, plenty of air should be given with the ethyl-chloride, and the spray can be easily controlled. No hard and fast rule can be given as to the quantity of ethyl-chloride which should be sprayed on to the gauze, the distance from the face, the depth of the child's respiration, and the temperature of the room, all being factors which will determine the amount which the child will actually inhale; and this will have a varied relation to the amount which leaves the ethyl-chloride spray. By giving plenty of air, which is assured by this open method, administration of oxygen is never necessary.

The stages of anæsthesia by ethyl-chloride have already been described. When the third stage is reached, respiration will be deep, perhaps stertorous, and the characteristic ocular signs can be demonstrated—widely dilated pupils, with the eyeballs rotated, generally downwards, but occasionally upwards. It is now that the face-piece may be removed and analgesia will be absolute for several minutes. The mouth should be opened by pressure with the palm of the hand on the chin in a downward and backward direction and a Mason's gag inserted in the region of the molar teeth. As muscular contraction has ceased, and relaxation has taken its place, there will be no difficulty in further opening the mouth with the gag. The dental surgeon will have from two to three and a half minutes during which time analgesia is absolute, and this will give him ample time without undue haste for the extraction of as many teeth as is necessary. It is not an unusual occurrence for sixteen teeth to be removed under anæsthesia thus induced.

This open method of inducing the ethyl-chloride anæsthesia for dental operations has quite superseded the closed method at the Hospital for Sick Children, Great Ormond Street. It has many advantages: there is considerably less post-anæsthetic vomiting, and muscular contraction is not quite so extreme during anæsthesia (probably due to the additional amount of air inhaled which is not so easily obtainable with the rubber bag), and the bag and face-piece of the closed apparatus are more often resented by the child than the simple gauze face-piece. In fact, it is entirely safe and a child seldom registers any objection to the induction.

In France the surgery of childhood is recognized as a definite "speciality," and the standard authoritative work in that country, compiled by the professor of this subject, has recently reached its third edition. Therein it is stated that chloroform is used in France for all operations about the mouth, because it is impossible to keep a child under with ether if the mouth is open; although it is added that in England it is "claimed" to be possible. It seems, therefore, to be all the more important that further attention should be drawn to the fact that the safety of ether over chloroform is so vast that the latter anæsthetic should never be permitted for children if any other procedure is at all possible. The two common operations when the child's mouth is wide open are (1) for tonsils and adenoids, and (2) for cleft palate. Of course, the former operation outnumbers the latter by many thousands, and, in fact, the operation for tonsils and adenoids so far exceeds in number any other operation in the surgery of childhood that it should be specially mentioned.

Many years ago, when the operation for the removal of tonsils by dissection was first devised by Mr. George E. Waugh, chloroform was used for the anæsthetic, and I can testify to the very real anxiety that I and others suffered in those days. The danger was a real one and it became obvious that some scheme, to enable ether anæsthesia to take the place of chloroform anæsthesia had to be devised in order to render this frequently performed operation perfectly safe for the child. It was found impossible to maintain deep anæsthesia by using ether in a Junker for two reasons: first, the afferent or centre tube became blocked almost immediately, owing to the low freezing point of the ether; and secondly, the bore of all the tubes was of insufficient size to enable enough ether vapour to come through the tube and reach the child. After numerous trials of various contrivances it was found that deep ether anæsthesia could be maintained so long as the anæsthesia was deep, to the extent of widely dilated pupils, *before* the face-piece was removed; and as long as the tubes, both the metal ones and the rubber ones which convey the ether vapour, had an internal diameter of not less than ¼ inch. Either air by means of a foot-bellows, or oxygen, was passed through a Woulfe's bottle. This bottle, placed in a vessel containing water, prevented blockage by freezing, and the ether vapour then passed through a lead coil, surrounded by hot water, thence by a rubber tube and malleable mouth-tube to the child's mouth. The apparatus complete is made by Messrs. Allen and Hanburys, and is used at the Hospital for Sick Children, Great Ormond Street, for all tonsil and adenoid operations. Deep anæsthesia by ether, with the child's mouth wide open, thus presents no difficulties.

SOME RECENT DEVELOPMENTS IN ANÆSTHESIA

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IN common with other branches of medicine, many important developments have taken place within the past five or six years in the practice of anæsthesia. Since 1927 a number of new anæsthetic agents have become available and a vast literature during the period under review has been concerned with assessing both their properties and the most desirable methods of administration. Whereas, in the past, progress in anæsthesia tended to proceed in the direction of better mechanical methods for the administration of volatile anæsthetics, the line of progress now appears to be directed towards improvements in drugs used to produce both general and spinal anæsthesia. In any circumstances, the comfort of the patient now receives full attention, and it seems that the vast majority of surgical procedures can be performed with the minimum of discomfort and with practically no increase in risk so far as the anæsthetic is concerned. It is difficult to single out any particular modern development in anæsthesia as especially valuable, but few will disagree that the use of carbon dioxide as a respiratory stimulant is probably the most valuable contribution recently made in this branch of medicine. For the purpose of this short survey it is convenient to classify modern developments in anæsthesia into three main groups: those pertaining (1) to the administration of volatile anæsthetics, (2) to basal narcotics, and (3) to spinal anæsthesia.

VOLATILE ANÆSTHETICS

Nitrous oxide.—At the present time nitrous-oxide-oxygen anæsthesia is employed far more frequently and for more severe surgical operations than ever before. Two circumstances probably account for this: first, an increasing number of administrators are experienced in this method of anæsthesia and use it with considerable success. Secondly, when nitrous oxide is used in combination with either basal narcosis or local analgesia a sufficient degree of muscular relaxation can be obtained for the majority of surgical procedures without the use of either ether or chloroform. Improvements in the design of continuous flow gas-oxygen-ether machines, particularly the fitting of flow-meters, permit more accurate proportioning of the percentages of gases employed, and the increasing popularity of machines of the intermittent flow variety allows considerable economy of gas. Furthermore, the use of well-fitting face-pieces minimizes leakages of gas and permits greater efficiency in administration.

An interesting development is the use of the closed circuit principle for administering nitrous oxide as described by Evans.[4] In this method nitrous oxide and oxygen are inspired from a rubber bag in the usual way and the interposition of suitable valves directs the expirations through a chamber filled with soda-lime. The expired carbon dioxide is absorbed by this substance and the expired nitrous oxide is readmitted to the inspiratory side of the apparatus from which it is used over and over again. Considerable economy results from the use of nitrous oxide by this method for, when once the necessary saturation point has been obtained, it is necessary to admit to the apparatus only sufficient gas to compensate for leakages. Cyanosis in nitrous-oxide-oxygen anæsthesia is usually regarded as undesirable, but Macklin[10] maintains that an asphyxial element is not harmful to the patient and produces deeper anæsthesia with complete muscular relaxation. It is necessary, however, to have an apparatus capable of instantly cutting off the anæsthetic supply and, if necessary, of inflating the lungs with oxygen and carbon dioxide.

Ethylene.—This gas, when given in combination with oxygen, secures far greater muscular relaxation than can be obtained with nitrous oxide. It is used commonly in America, but has never been popular in this country for several reasons; these are probably (*a*) difficulty in obtaining the gas, (*b*) its unpleasant odour, and (*c*) the risk of explosion—a risk which, provided adequate precautions are taken, is undoubtedly over-estimated.

Ether.—The preservation of ether from decomposition is important, and in this connection it has been shown that if this liquid is stored in copper-lined containers, it does not decompose. This principle has been extended by the use of copper or copper-plated tubes in the Boyle and similar machines. The most promising recent developments in ether anæsthesia, however, have been those concerned with its endo-tracheal administration. This method has been employed for many years and the usual practice is to conduct nitrous oxide and oxygen with or without warmed ether vapour into the trachea through a small-bore catheter, which itself is introduced through the mouth and larynx under direct vision with the aid of a laryngoscope. The expired gases escape to the external air through the free space between the catheter and the tracheal wall. If any difficulty is anticipated, either in maintaining the air-way or in preventing aspiration of foreign materials, it is advisable to introduce a second catheter alongside the first in order to carry away the expirations. Gauze can then be packed round the tubes and the air-way is maintained with no risk of fluids being inspired.

Magill[11] has introduced a simple and effective method of intubation (termed " blind intubation ") in which the catheter is inserted through the nose instead of through the mouth (*see* page 431).

Waters[19] has described a method of preventing fluids entering the trachea in which a wide-bore catheter is passed through the mouth in the usual fashion. This carries, at a short distance from its tracheal end, a small rubber cuff which is capable of pneumatic inflation and effectually seals the interval between the catheter and the tracheal wall.

Chloroform.—Thompson Rowling[16] has described a simple apparatus for determining the percentage of chloroform vapour inhaled. It is extremely useful for the anæsthetist to know this strength, and hitherto the only available method has been by the use of Vernon Harcourt's or similar apparatus. Briefly, Rowling's method consists of bubbling air through a mixture of chloroform and liquid paraffin in which balls of varying specific gravities are immersed; chloroform is carried off from the mixture, and its specific gravity falls. The maximum strength of chloroform vapour which can be obtained from the mixture is 3·5 per cent., and the specific gravities of the balls are adjusted so that they fall, one by one, as the percentage of chloroform in the mixture diminishes. The need for a safe and reliable analgesia which can be administered by the midwife during childbirth has led Rivett[14] to recommend the use of capsules containing 20 minims of chloroform. One of these can be crushed and placed on the mask as required, and it is believed that analgesia can safely be obtained without undue risk.

Divinyl oxide.—From time to time new anæsthetic agents are introduced, but investigation of their properties shows that they are neither so reliable nor efficient as those they are proposed to supersede. Divinyl oxide, however, appears to be a promising recent introduction; it is a clear liquid which is more volatile, but not more explosive than ether, possesses a sweetish ethereal odour, and is comparatively non-irritating to the respiratory tract. Experiments by Gelfan and Bell[6] indicate that induction is smooth, prompt and even;

muscular relaxation is good and there is a rapid recovery period with very little nausea. They believe that this substance is worthy of an extended trial as an anæsthetic.

Carbon dioxide.—Although carbon dioxide cannot be termed a volatile anæsthetic, it may be mentioned in this connection because it is administered by inhalation. It is interesting to reflect that though the effect of carbon dioxide upon respiration has been known for many years, it is only recently that this gas has been employed in anæsthesia and general medicine, as a respiratory stimulant. Nevertheless, Clover's inhaler makes use of the principle involved, the expired carbon dioxide being collected in the bag and used to stimulate respiration. Carbon dioxide is pre-eminent as a respiratory stimulant and, in cases of respiratory failure, has superseded the administration of lobeline and other drugs. Mixtures containing upwards of 10 per cent. carbon dioxide with oxygen are used in anæsthesia, particularly ether anæsthesia, in order to promote more rapid excretion of the anæsthetic and also to induce deep respiratory movement and so minimize the risk of post-operative pulmonary complications. The gas can also be used during induction to stimulate respiration in a recalcitrant patient. The value of carbon dioxide as a respiratory stimulant is not confined to anæsthesia, for it is useful in any illness in which an increase in the respiratory exchange is desirable.

BASAL NARCOSIS

Although only recently coined, the term " basal narcosis " implies nothing new in the practice of anæsthesia. Long before the properties of the common inhalation anæsthetics were discovered, opium, cannabis indica, and other drugs were employed to produce the effects which are now secured by the administration of certain complex chemical compounds. Basal narcosis means that the patient shall be rendered insensible by the use of a non-volatile anæsthetic, and that, if the narcosis so produced is not sufficiently deep for the proposed operation, full surgical anæsthesia can be obtained by the superimposition of an inhalation anæsthetic. The advantages of this method from the patient's point of view are three-fold: (1) induction is pleasant and there is little or no psychic shock; (2) the pharmacological properties of the drugs employed indicate that surgical shock will be minimized; and (3) the recovery period is prolonged and the risk of post-operative vomiting is minimized.

In comparison with inhalation anæsthetics, all basal narcotics have the disadvantage of slow absorption and excretion. With inhalation anæsthesia, it is easy to maintain the patient at a constant level of anæsthesia without the risk of over-dosage because the large vascular area available in the lungs allows rapid exchanges, but with non-volatile anæsthetics, absorption and excretion are necessarily slow and the level of anæsthesia must be maintained by the administration of a single dose. Accordingly, when once a non-volatile anæsthetic has been administered it is impossible to control its action further, and this fact indicates that it is of prime importance to gauge the dose according to the patient's requirements.

Non-volatile anæsthetics which are used to produce basal narcosis can be given either by the mouth, the rectum or intravenously, the choice of method being governed by the properties of the individual anæsthetic. These substances may be divided into three groups: (1) liquids with too high a boiling point for administration by the lungs, for example, paraldehyde; (2) alkaloids, such as morphine and hyoscine; and (3) solid substances, often very insoluble in water, which act by virtue of lipoid solubility. This group includes chloral and its various derivatives; sulphonal and methyl sulphonal; veronal and its derivatives, medinal, luminal, pernocton, amytal and nembutal; urethane with its derivative, hedonal, and the organic bromine compound, avertin. All these drugs are excellent hypnotics and have been used from time to time as basal narcotics, the most popular until recently being paraldehyde. The majority are unsuitable as anæsthetics because the therapeutic margin is insufficient and the present value of basal narcosis is due to the introduction of four substances, namely, avertin, amytal, nembutal, and pernocton, which possess both a far greater therapeutic margin than their predecessors and also several practical advantages. Avertin is usually administered by the rectum, amytal and pernocton intravenously, while nembutal can be given either intravenously or by the mouth.

Paraldehyde.—This liquid, which has been employed as a basal narcotic for many years, has recently been overshadowed by avertin and the barbiturates. Stewart[17] relating his experiences of 500 administrations believes that it provides a safe and certain method of eliminating for the patient the more unpleasant accompaniments of operation and that it facilitates the anæsthetist's task without adding to his anxieties. He administers paraldehyde dissolved in normal saline solution by the rectum and finds that sleep supervenes in a very short time while the recovery period is prolonged for from five to eight hours. The unpleasant odour of paraldehyde, which is excreted by the lungs, is, apparently, not noticed by the patient; post-operative restlessness is uncommon and there is no fall in blood pressure after its use. Stewart states that, in respect of safety and certainty of action, paraldehyde premedication compares favourably with that effected by other basal narcotics.

Avertin.—Avertin is a reduction product of bromal and it is said that its anæsthetic properties were discovered accidently while endeavouring to produce a derivative of this substance as a remedy for whooping cough. It is a true anæsthetic and not merely a narcotic, for it will cause both insensibility and immobility. In the human it is usually administered in aqueous solution by the rectum, but the intravenous route is also effective. In any case it is important to ascertain that this solution is properly prepared because, otherwise, decomposition products are formed which, if injected, produce irritation. Administration is quite simple; it is unnecessary to wash out the rectum either before administration or after the operation. The appropriate dose is run in slowly and in ten minutes the patient begins to feel drowsy; he passes into a deep sleep and in a further ten minutes the corneal reflex is usually abolished and he is fit to be taken into the operating theatre.

To those without experience of the effects of the drug, the appearance of the patient at this stage is rather bewildering. The countenance is ashen and sometimes there may be a suspicion of cyanosis. Respiration is inaudible; it is very shallow, but the rate usually remains normal, and this depression is due to a specific action of avertin upon the respiratory centre. If the dose has been accurately calculated the centre will respond to afferent stimuli, such as mechanical stimulation or the inhalation of ammonia, ether or carbon dioxide, and there is not any inherent danger in this type of respiration. The jaw sags and the muscles are remarkably flaccid; the pupils are contracted to a pin point; this is a central effect and, provided the dose is within safe limits, passes off with the application of external stimuli. The pulse remains of good volume and its rate is unchanged. The systolic blood pressure falls slightly, about 10–15 mm. of mercury, this probably being no more than occurs in normal sleep. This is one of the great advantages of avertin—in ordinary doses it is without appreciable action upon the cardio-vascular system, as can be shown experimentally, and therefore it can be selected when disease of the heart or blood vessels contra-indicates the employment of an alternative anæsthetic.

Although the corneal reflex has been abolished and the patient appears to be in an ideal condition for the operation to commence, it will be found, in the majority of cases, that the insertion of towel-clips produces reflex movements; if this occurs it is necessary to administer an additional anæsthetic and, as a rule, gas and oxygen is sufficient. Some cases require no additional anæsthetic while others require the addition of ether, and this emphasizes the variable effect of avertin in different individuals and the need for careful judgment in dosage.

The anæsthesia is very satisfactory for the surgeon; muscular relaxation is complete, there is the minimum of bleeding, while the diminished excursion of the diaphragm is of value for abdominal surgery. The patient appreciates avertin because it abolishes the discomfort of induction, while after-effects are not unpleasant. The recovery period is prolonged, but it is difficult to say for how long because so frequently the patient passes into more or less natural sleep, from which he can be roused easily. In common with other basal narcotics the patient usually presents a far more comfortable post-operative condition than is seen after the administration of ether or chloroform. Vomiting does occur, but its incidence is not so great, neither is it of such intensity. Restlessness, however, occurs, but personal experience indicates that the incidence of this is not so common as with the barbiturates.

When avertin was first introduced it was given in much larger doses than at present in an attempt to produce anæsthesia without the use of volatile anæsthetics. With this object in view, morphine and various derivatives of barbitonum were freely employed, sometimes in large quantities, both as premedicaments and as adjuvants. Realization of the fact that these drugs in conjunction with avertin caused profound respiratory embarrassment and also that deaths attributable to avertin occurred usually when they had been given has indicated that it is inadvisable to employ them. The only premedicament necessary is atropine in appropriate dosage. In this connection it is necessary to refer to amylene hydrate. Avertin is a powder relatively insoluble in water, and accurate weighing and dissolving constitute real practical difficulties. To obviate this, avertin is now sold dissolved in amylene hydrate, a malodorous liquid which itself possesses anæsthetic properties and is also a potent respiratory stimulant.

Avertin is detoxicated in the liver and the compound which is formed in this organ is excreted slowly by the kidneys. There is evidence[7, 20] that avertin damages the liver, but this view has been questioned[1, 2]. Regarding its effect upon the kidneys, it is stated[18] that the tolerance of animals subjected to experimental nephritis to avertin is considerably reduced, and therefore caution should be exercised in administering this substance to patients with renal damage.

Avertin is of particular service to the surgical treatment of Graves' disease. For some reason these patients can take much larger doses than are usually employed and it is believed that the excess of thyroxine present detoxicates the drug and minimizes the risk of toxic symptoms. In any case it allays the psychic distress which they so commonly experience, and the absence of deleterious effects upon the cardio-vascular system gives confidence to both surgeon and anæsthetist.

Present opinion indicates that avertin is an extremely useful addition to the range of anæsthetic agents available for the administrator, and a personal experience of over 400 administrations in selected cases which have not given rise to any anxiety confirms this view. Nevertheless, occasions may rise when it is considered desirable to interrupt avertin narcosis, and both coramine[9] and ephedrine[13] have been found suitable for this purpose.

THE BARBITURATES

Three derivatives of barbituric acid have been used extensively as basal narcotics. These are sodium amytal, nembutal and pernocton, and it is stated that they have the following points in common[21]: (1) There may be very considerable variation in the observed effects when given in the same dose to the same species; in other words, the variability of action has made it difficult to secure an accurate scale of dosage. (2) In hypnotic doses they may produce respiratory and circulatory depression. (3) During the processes of destruction and excretion, certain products are formed which may produce mental disturbances and restlessness. These may persist during the period of excretion which may occupy several days.

Sodium amytal.—This is a white crystalline powder which is given intravenously in aqueous solution. The method of administration is peculiar; the solution is freshly prepared and is then injected at the rate of 0·1 gram per minute until the patient fails to answer to the spoken word. When the injection is completed. inhalation anæsthesia is superimposed as with avertin and both gas and oxygen or ether may be used for this purpose. Sodium amytal depresses the cardio-vascular system more than avertin does; the systolic blood pressure falls to 30 mm. Hg or more; the diastolic 15 mm. mercury or more and the pulse-rate always rises considerably. Respiration is depressed to a less extent than is seen with avertin but, on the other hand, reflex excitability is at a much lower level.

Nembutal.—Nembutal (sodium-ethyl-methyl-butyl barbiturate) is more toxic than sodium amytal and therefore can be given in smaller doses to produce a similar degree of narcosis. As the dose is smaller, detoxication is accomplished in a shorter time and therefore the recovery period is not nearly so long as with sodium amytal, the recovery period of which may extend to 24 hours. This drug can be given either intravenously or by the mouth; the former method is identical with that employed for sodium amytal, but as the dose is only half as large, administration occupies only 7 or 8 minutes. When nembutal is given by the mouth an attempt is made to correlate the dose with the body weight but this does not lend itself to the accurate results which can be obtained by the former method. When given by the mouth, the patient falls asleep in about 20 minutes and there may be narcosis in a further 10 to 20 minutes. There is usually nystagmus and very frequently strabismus at this stage; an effect which is common to all derivatives of veronal in heavy dosage. There is usually some twitching of the limbs and also a peculiar flickering of the eyelids. Muscular relaxation is not nearly so marked as with avertin, but there is a greater degree of insensibility. For example, when a patient has been given the appropriate dose of nembutal by the mouth, induction can be completed and anæsthesia maintained with open ether with very little change in the rate or amplitude of respiration. This function is not greatly depressed by nembutal, the only apparent difference being a decrease in the depth of respiration. The fall in blood pressure ranges from 20 to 30 mm. Hg, but this tends to rise again in a short time.

Regarding after-effects, the recovery period after oral administration is comparatively short and seldom extends beyond 3 hours. Not infrequently excitement occurs during this time and involuntary movements of the limbs, together with shouting may be observed. The incidence of post-operative vomiting is no greater than with avertin. With intravenous injection Boyd[3] states that the full hypnotic effect, when produced, lasts 4 to 5 hours and for a further 12 or more hours the patient is peacefully asleep.

O'Sullivan and Craner[12] advise the use of nembutal and chloral hydrate as an analgesic in childbirth. Three grains of nembutal are given by the mouth followed by 30 grains of chloral hydrate. Either or both of these can be repeated in modified doses after 2 hours and additional doses may also be given. Usually a painless labour results, but this process may be prolonged and may be succeeded by restlessness.

Pernocton.—Pernocton, the last member of this series, is the sodium salt of secondary beta-bromallyl barbituric acid, and it is issued in ampoules already dissolved in water. Its hypnotic effect is comparable with that of nembutal but it is effective in smaller dosage. The average quantity of pernocton necessary to produce narcosis is 4½ grains; this amount is contained in 3 c.cm. of solution, which, when administered intravenously, at the rate of 1 c.cm. per minute, can be injected in 3 minutes and still further shortens the induction period when compared with nembutal. Administration of pernocton is conducted in precisely the same manner as with the two previous drugs and unconsciousness supervenes before the needle is withdrawn. Pernocton anæsthesia resembles that produced by nembutal, but it is stated[15] that vomiting and excitement are prone to occur. The recovery period is said to be from two to six hours.

It is probable that nembutal is the most commonly employed barbiturate at the present time. The oral method of administration is most convenient, but it is difficult to form an accurate estimation of the necessary dose. The intravenous route gives excellent results and is preferred by many administrators, but according to the Council of Pharmacy and Chemistry of the American Medical Association[22] it is subject to the objection that all barbiturates require large quantities of alkali for solution and, therefore, they will not remain in solution in the blood stream. They are believed to be precipitated and to circulate as foreign bodies in the colloidal state.

SPINAL ANÆSTHESIA

For many years drugs of the novocaine group have been employed as spinal anæsthetics and for this purpose small quantities of a strong solution of the selected drug have been injected into the cerebrospinal fluid. When the injection is made by the usual lumbar puncture it is difficult to ensure that the anæsthetic effect will reach a sufficient high level of the spinal cord, but this object can be achieved in one of three ways[5] :—(1) by injection at the upper level of the nerve-roots to be paralysed; (2) by injection in the lumbar region and reliance on gravity to carry the drug to the level required; or (3) by barbotage or mixing the drug in the syringe with cerebro-spinal fluid withdrawn and injection of this mixture.

The whole position regarding spinal anæsthesia has been changed by the introduction of percaine, which is a derivative of quinoline, being the hydrochloride of a-butyloxycinchoninic acid diethylethylendiamide. It it a considerably more powerful anæsthetic than cocaine, but it is stated to be five times more toxic. As, however, it acts in a dilution of one in 1500 the net result is that it is safer than cocaine. The solution for spinal use is made with 0·5 per cent. saline and this gives a specific gravity less than that of cerebro-spinal fluid. It acts in the presence of inflammatory exudates but it is precipitated by alkali.

Howard Jones[8] has evolved a very successful technique for spinal anæsthesia which is dependent upon the low dilution in which percaine is effective. The subarachnoid space is treated in the same fashion as the tissues in infiltration anæsthesia and 10 to 15 c.cm., according to the level which it is desired to anæsthetize, are injected directly into the subarachnoid space by the usual lumbar puncture. For lower abdominal operations below the umbilical level, 10 c.cm. are usually sufficient while 14 c.cm. will provide excellent anæsthesia for upper abdominal operations. With

Howard Jones's method, the anæsthetizing agent does not diffuse upwards into the cerebro-spinal fluid and so affect the cord to an undetermined level, but it bathes this structure in proportion to the quantity injected. The inevitable fall of blood pressure can be counteracted by the injection of ephedrine. Although the method outlined above gives excellent results and the upper limit of activity can be controlled with reasonable accuracy, there is no reason why percaine should not be used in greater strengths by the older method of barbotage. The disadvantages of percaine when used for spinal anæsthesia are similar to those obtaining when any other drug is employed. It is stated that its toxity is negligible, but from time to time reports are made which indicate that death has been due to administration of this substance. It is probable, however, that in these cases death would have occurred if any other spinal anæsthetic had been employed.

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THE USE OF EXTRACT OF SUPRARENAL CORTEX IN ONE TYPE OF NEURASTHENIA

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EVERY physician must have noticed the great similarity between some cases of neurasthenia and early cases of Addison's disease. During the last few years I have had opportunity of making observations upon the effect of treating selected cases of neurasthenia with intravenous injections of an active extract of suprarenal cortex. The results have been sufficiently promising to justify a therapeutic trial upon a wide scale, extreme care being taken that the patients are investigated in sufficient detail to be sure that they belong to a certain type. If all cases of neurasthenia are treated with injections of cortin the results will be disappointing and the method will be discredited.

Before recording in detail the method of arriving at the diagnosis of the type which depends upon inadequacy of the suprarenal cortex it is necessary to explain the meaning of the word "neurasthenia" as used in this article.

The terms hysteria and neurasthenia have been used extremely loosely to cloak the ignorance of those who have not had the courage to admit want of knowledge. It is not so very long ago that septicæmia following childbirth was termed hysteria, and at that time the medical profession were in the habit of prohibiting the tolling of church bells at the funeral of a victim lest other parturient women might learn the cause of the tolling, develop and die from a similar hysteria. "Neurasthenia" should mean a nervous system of abnormally easy fatigability. Freud would limit the meaning of the term to the symptoms resulting from excessive indulgence in the sexual act. Whatever our view of Freud's teaching, we must all render homage to him for insisting upon the possibility of discovering the causes of all the weird manifestations which in the past many have been satisfied to term "functional."

The symptoms of neurasthenia are physical and mental fatigability with a poor power of concentration along with mild gastro-intestinal disturbances. These symptoms are common in most severe diseases, but nevertheless the term would not be applied to a patient suffering from advanced tuberculosis who develops them, and the term has been reserved for those cases in which a cause cannot be found. At the present day most authorities would agree that there is a physical basis for the majority of cases of neurasthenia, and this article draws attention to one cause only, and probably one which is far from the most frequent. It may be of interest to see how the cause has been arrived at by reviewing the effects of destruction or complete atrophy of some of the internal secreting glands and comparing them with the syndromes associated with inadequacy.

Thyroid gland.—Destruction, removal or complete atrophy of the thyroid gland leads to death due to a great reduction in the power of resisting microbic infection associated with slow metabolism, thickening of the subcutaneous tissue, changes in the hair and impairment of memory. Thyroid inadequacy, if very slight indeed, may cause a gain in weight along with a loss of initiative, without other signs.

Pancreas.—Destruction or complete atrophy of the internal secreting cells of the pancreas leads to death from diabetes mellitus preceded by severe thirst, polyuria, wasting and the production of poisons resulting from the alteration in metabolism, poisons which cause coma and heart failure. Mild inadequacy leads to hyperglycæmia accompanied by glycosuria after meals rich in carbo-hydrate. Occasionally careful investigation is required to detect the inadequacy.

Parathyroid glands.—Destruction or removal of the parathyroid glands causes tetany, restlessness, coma and death. Mild inadequacy may be manifested by cramp, chilblains and restlessness, and can be proved only by determining the calcium content of the blood.

Pituitary gland.—Complete atrophy of the pituitary gland leads to impotence, emaciation, cachexia and death, and mild inadequacy to syndromes depending upon which cells in the gland have had their activity diminished.

Suprarenal cortex.—Destruction or complete atrophy of the suprarenal cortex leads to death preceded by pigmentation of skin and mucous membranes, listlessness, myasthenia, low metabolism, low blood pressure, low temperature and low sugar-content of the blood. Cortical inadequacy has not been generally recognized. In the past, when the diagnosis of suprarenal inadequacy had been made and the patient had survived for years, it has been assumed that the diagnosis was incorrect. Inadequacy of these glands would be expected to lead to the symptoms of neurasthenia associated with low temperature, low sugar-content of blood, and low blood pressure. It is obvious that one can expect amelioration to follow the injections of an active extract of suprarenal cortex, if limited to those cases which present signs of impaired activity of that tissue.

An obvious argument against my contention is that neurasthenics recover, whereas patients with Addison's disease usually die within five years of onset. I hope to prove that this argument is fallacious.

The adequacy of a gland depends upon various factors and is not a fixed activity. This may be illustrated in many ways. For instance, a patient suffering from diabetes mellitus may be placed upon a fixed diet and doses of insulin which maintain the sugar-content of his blood between the limits of 0·15 per cent. and 0·08 per cent. throughout the twenty-four hours for weeks or months, until one day he is called upon to carry out prolonged muscular activity which leads to the concentration of sugar in his blood falling to 0·04 per cent. and the development of hypoglycæmic symptoms. Later the same individual may develop pyorrhœa or some other infection, and then the sugar-content of his blood may rise to 0·25 per cent. or higher, and he may need much larger doses of insulin to maintain his health, or if the infection happens to be of a certain type his metabolism may be affected so profoundly as to lead to ketosis and coma.

A similar series of circumstances may affect a case of Addison's disease, except that increased muscular activity calls for an increase in the subsidy for the inadequate suprarenal cortex. An infection, however, may hurl the patient to or even through the gates of death, depending upon the possibility of supplying a sufficiency of the active principle. When the infection has passed, the patient may be able to live a quiet, sheltered life without injections of cortin. These cases disprove the notion that when there is once inadequacy of a gland there is always inadequacy of that gland.

Neurasthenia frequently follows some illness and occasionally is attributed to some slight infection, such as pyorrhœa or infected tonsils; when the infection is removed the patient makes a slow recovery. This is in complete keeping with the view that symptoms arise from inadequacy of the suprarenal cortices, the action of which is further impaired by the toxins absorbed. When a focus of infection can be detected it should be removed without delay, occasionally injections of an active extract of suprarenal cortex may accelerate recovery. This impairment of function due to toxins is not confined to the pancreas and suprarenal cortex: it is found that when a case of diabetes insipidus is controlled by 10 units of pitressin daily the dose may have to be increased to 30 or even more if an abscess develop or certain micro-organisms invade. A similar effect is produced by infection in cases receiving parathormone for parathyroid inadequacy.

There may be yet another reason for the necessity for only temporary treatment. Rest of a diseased gland may assist in regeneration. This is shown occasionally when a case of diabetes mellitus with acute onset is treated with insulin in adequate doses within a few days of the onset. Within a few weeks or months insulin is no longer required.

I think, therefore, the argument that neurasthenics recover whereas patients with Addison's disease die is no evidence against the theory that the cause of neurasthenia in a certain percentage of cases is due to inadequacy of the suprarenal cortices. The examination of the patient is comparatively simple. The blood pressure should be taken with a reliable instrument, preferably a self-recording sphygmomanometer, because it removes the personal factor from the observer. It is true that it often records a pressure somewhat higher than that which is found by the auditory method, but that is an adverse criticism of the auditory method and not of the machine. It is also true that readings taken within a short time of one another are not all the same; this, too, is not an argument against the method, but proves that the blood pressure in some individuals changes from minute to minute. Before arriving at the conclusion that the blood pressure is abnormal it should be taken upon several occasions. If the self-recording instrument shows that it is consistently below 110 mm. Hg it is safe to assume that it is below the normal average.

The concentration of sugar in the blood should be estimated in two samples at least, one three hours after food and another one hour after a meal rich in carbohydrate. If the former is under 0·07 per cent. and the latter under 0·14 per cent. the blood may be considered to contain less than the normal average. This by itself is of no diagnostic value, but only confirmatory. The temperature should be taken when the patient is in bed and has been without hot-water bottles for a considerable period. Patients with inadequacy of the suprarenal cortices have a slow metabolism and feel cold, and therefore insist on hot-water bottles whilst in bed, hence the necessity for the precaution mentioned. If the mouth temperature is 97° F. or below and the other signs are present and the patient complains of muscular fatigue, treatment with cortical extract is justifiable, even if a definite myasthenic reaction is not obtainable by methods more crude than the ergograph, which is not always at one's disposal. The patient may be asked to grip a dynamometer at intervals of two seconds, and if the power of the grip falls rapidly, myasthenia is demonstrated.

Any method of treatment which is expensive may lead to improvement through suggestion. At one time neurasthenia was treated with a serum prepared from lymphatic glands which cost a guinea a dose, and no doubt benefited patients who were aware of its cost. An attempt should be made to differentiate between the effect of suggestion and that due to the physiological action of a drug. This I have attempted to do by telling some patients that the treatment was experimental or by assuring them that the effect of the injection is practically instantaneous, so that if the effect were due to suggestion they would acknowledge improvement straightway, but in no case has the patient admitted benefit until after the fourth injection.

I have given the extract intravenously in doses of 2 c.cm. on alternate days for two or three weeks. I have also tried it in cases which appeared to be suffering from neurasthenia but without the signs of suprarenal inadequacy, without obtaining any effect whatsoever. In Addison's disease the signs of improvement are demonstrated primarily by the general condition of the patient and secondarily by the loss of myasthenia and a rise in the temperature, while the blood pressure and sugar-content of the blood may both remain well below the normal average. In neurasthenia treated successfully by injections of an active extract of suprarenal cortex improvement is shown by the return of muscular and mental energy and the temperature approximating the normal, but the blood pressure and sugar content of the blood do not rise invariably. In suitable cases the result may be astonishing, changing a listless individual who spends the day on the sofa into one who radiates energy, works all day and plays half the night.

CANCER : A REVIEW OF MODERN TREATMENT

By PERCIVAL P. COLE, F.R.C.S.
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I HAVE been associated with the study of cancer and with the Cancer Hospital for some twenty years and, although my experience of carcinoma is very largely surgical, have had the opportunity of observing the outcome of a number of vaunted cures recommended either in the medical press or at the instance of individuals who have been alleged to have discovered a treatment. It is impossible in a short article to deal with all the cancer cures put forward from the earliest days of empirical medicine. I propose, therefore, to deal with some aspects of cancer that have come under notice during my professional life.

It has been stated, and there is some evidence in favour of the view, that cancer is on the increase. That the total number of deaths ascribed to cancer has increased cannot be denied.

The total number of cancer deaths in males in 1921 was 20,649, whereas the corresponding figure in 1928 was 26,013. The total cancer mortality in females in 1921 was 25,373, whereas in 1928 it amounted to 30,240, thus giving a total death rate of 46,022 in 1921, and 56,253 in 1928. In connection with the larger number of deaths in females, it must be remembered that the female population in these two periods exceeded the male population by about 1,700,000. The apparent increase in cancer deaths therefore roughly amounts to 10,000. There are, however, other factors that demand consideration; thus, the total population is increasing; in 1921 it was 37,887,000 and in 1928 39,482,000, an increase of nearly 2,000,000. Again, the number of patients dying before the age of 40 has steadily diminished; in 1921, deaths before this age amounted to 170,197, in 1925 to 149,093 and in 1928 to 128,924. The total number of deaths for the corresponding years are as follows ; 1921, 458,692; 1925, 472,841; 1928, 460,389. It is clear that a steadily increasing number of people are attaining the age of 40, the age at which, for practical purposes, the risk of cancer begins. The factor of diagnosis also has a bearing; owing to better educative methods and the increasing interest in the cancer problem, knowledge of the disease has become more accurate; more deaths may, therefore, be expected to be rightly attributed to carcinoma, and, as a natural corollary to extended zeal, it is probable that many deaths are attributed to it erroneously.

To sum up the position, it may reasonably be urged that cancer is not on the increase; but it cannot, unfortunately, be said that cancer mortality has diminished. The position may be compared with that which obtains in the case of tuberculosis, a disease which preventive medicine has been able to influence favourably to some extent. The total deaths from tuberculosis in 1921 were 42,698; in 1928, 36,623! There is thus a diminished mortality of about 15 per cent. in seven years. This comparison is introduced because the causal factor of tuberculosis is known. In certain quarters it is assumed, and I suggest wrongly, that the discovery of the cause of cancer will eventuate in the extermination of the disease; an hypothesis not borne out by the known facts relative to tuberculosis.

In connection with the hypotheses advanced touching the pathological factors involved in causation, it may be of interest to refer to the work of Gye and Barnard published in 1928, and to Gye and Purdy's recent book[1] in which a plea for the parasitic theory is advocated. Little can be gained by spending time or energy on the discussion of academic hypotheses, but one important item in connection with causation and the wide-spread and oft-times ridiculous suggestion relating thereto, may be mentioned. A connection between cancer mortality and some other variable is, or may be, interpreted in certain quarters, particularly in the columns of the sensation-mongering press, as equivalent to a causal relation, provided such an assumption is not tacitly absurd. It will be pertinent, in this connection, to state that an intensive investigation carried out for the Ministry of Health on the causal relation between flesh diet and incidence of cancer, clearly indicated that no such causal relation could be established.[2] The investigation concerned the diet and the incidence of cancer amongst religious and segregated societies who eschew a meat diet either very largely or entirely. The societies involved in this investigation included Carthusians, Benedictines, Cistercians, Carmelites and Dominicans; and, in connection with this investigation, it will not be inappropriate to cite the candid expression of opinion voiced by the investigators:—

> "Nobody, of course, argues that the increase during the last quarter of a century of the Socialist Party has been an etiological factor of the increasing mortality from cancer, because no rational person can imagine any direct relation of cause and effect between the two variables. Substitute consumption of meat, margarine or tinned foods, and many intelligent people would accept the proposition as valid. The statistical argument is precisely as good in one case as in the other, and supports the suggestion that from the statistical standpoint, all these things may be factors in the alleged increase in cancer mortality."

Finally, it is stated that the analysis completely proves that fatal cancer occurs in populations abstaining from flesh foods and lends no real support to the contention that among such populations the relative incidence of cancer is low.

> "We think," say the investigators, "a perusal of our report will convince most impartial persons that no scientific value whatever, attaches to assertions supported merely by the vague, pseudo-statistical evidence which is erroneously cited respecting the rôles of certain articles of common consumption in the genesis of cancer. There is a too general impression that it is the duty of scientific men to try out any and every suggestion of this kind. As the present report abundantly proves, the trying out of any such suggestion is a most laborious business, not merely for the investigators, but for the persons called upon to supply information. Such a task ought not to be imposed without strong reason."

The application of remarks such as these to an institution such as the Cancer Hospital is obvious. We are constantly being importuned to try out this cure or that, the value of which may be supported by claims which are merely personal and somewhat vague or, on the other hand, the methods commended may be supported by authority and evidence of varying weight.

The first nostrum which attained to any degree of prominence in my professional life was claimed as specific both for diagnosis and cure by the French surgeon Doyen, at the beginning of this century.[3] He maintained that his *Micrococcus neoformans* was not only the causal factor in the production of cancer, but that agglutination occurred only in cancer patients. On the strength of these assumptions, he formulated not only a cure for cancer, but a method of diagnosis. His findings were severely criticized by his colleagues in France; the alleged cancer growths produced by him as the result of experimental work on animals were shown to be not carcinomatous but inflammatory, and agglutination was conclusively proved to take place, not only in other diseases in human beings, but as a normal process in animals. It is interesting to note that representatives from the Cancer Hospital were despatched to Paris to investigate on the spot the claims put forward by Doyen, and their report to the authorities of the hospital confirmed absolutely the destructive criticisms of his own *confrères*.

Since that time, the research and clinical departments of the Cancer Hospital, additional to other activities essential to their routine work, have tested and assessed the value of many methods destined by their originators to cure cancer or to alleviate its symptoms and prolong life. I propose merely to tabulate a series of methods for the cure or alleviation of cancer which have been investigated at the Cancer Hospital by Dr. Stanley Wyard. These include procedures of a purely empirical nature and others supported by pathological and clinical data. In all cases the results have shown these methods either to be valueless or so uncertain in their action that their use has been abandoned. They are: viscum album, Antimeristem and Novantimeristem, Cardigan cancer cure, vitamin-free diet, Coley's fluid, pituitary extract, Koch's serum, colloidal copper, colloidal selenium, colloidal lead, colloidal lead selenide, and irradiated fluorescein.

The latest addition to attain to a degree of publicity was that associated with the name of Dr. Bendien. His claims were investigated in the research, pathological and physics departments of the Cancer Hospital, and in the annual report of this hospital, relative to this subject, it is stated: "The summer and autumn months of the year were largely occupied in spectroscopic researches into the alleged discovery by Dr. Bendien of a new method of diagnosing cancer from the blood of patients. It has unfortunately to be reported that these claims could not be substantiated."

Heat.—I have had considerable experience in the application of heat as a method of dealing with such carcinomas as are suitable by reason of their site. These may be particularized as occurring in the uterus, either the cervix or the body and the maxillary antrum. In both cases it has been my custom latterly to combine this treatment with the use of radium in the form of surface applications or the insertion of needles directly into the tissues either at, or subsequent to, the application of heat. Byrne, of Brooklyn, towards the end of the last century, drew attention to this method of dealing with early carcinoma of the cervix by means of the galvano-cautery, at a time prior to the introduction of the radical Wertheim operation.[4] Percy drew attention to a more scientific method of applying heat, his original paper appearing in 1912.[5] He demonstrated his method at the Cancer Hospital in 1913 when I was detailed to assist him. Modifications in the technique have since been introduced in order to ensure a greater measure of control, and to eliminate untoward complications such as the occurrence of severe secondary hæmorrhage. It may be of interest to note that the reasons regulating the application of heat in the manner indicated are, in bulk, precisely similar to those which have been formulated in the case of radiations, particularly the gamma rays of radium. Heat, applied as has been done by Percy and myself, has, as its objective, a purely destructive action over a relatively limited area. Its main rôle is selective and is based on the alleged sensitivity of the carcinoma cell to a temperature lower than that which is destructive for the connective-tissue cell. Thus, it is stated that the carcinoma cell is destroyed when the temperature of the mass in which it lies is raised to 122–132° F., while the vitality of the normal tissues is not changed till the temperature attains 130–140° F. In an exhaustive paper by Westermark[6] on the effect of heat upon rat tumours, it is shown that heat has a selective and destructive action. The time factor, moreover, is dealt with in detail and it is shown that at a temperature of 47–48° C. recession takes place after exposure for 20 to 30 minutes, a period which can reasonably be determined in the circumstances necessarily attending the treatment of carcinoma in the human being. It may be admitted that radium, with its selective action on the cancer cell, has superseded this method and I rarely use it.

Heat, in common with X- and gamma rays, is a form of energy and, moreover, under suitable conditions, is in common with these radiations, a destructive agent. The amounts of energy involved in the two cases are very different; for example, a dose of X- or gamma rays, capable of considerable destructive action, would correspond in energy measure to a rise in temperature of the tissues of the order of only one thousandth of a degree Centigrade, whereas this rise caused by simple heating would, of course, bring about very little change in any living tissues. This fact points to a fundamentally different mode of action, X- or gamma rays bringing about their changes by intense but very local ionizations, whereas the application of heat will result in changes in all the chemical molecules involved. (Possibly intense cold would have similar effects.) Granted selectivity in the two cases, the use of heat as the destructive agent may justly be regarded as a "scientific" procedure, exactly as the employment of radiations, provided that the appropriate techniques are worked out in the two cases. Suffice it to say, that from the practical aspect, some of the results have been equal to any that have been obtained by radiotherapy.

Heat has been applied for the removal or destruction of carcinomatous lesions in another form, that of surgical diathermy; and although no cures in the true sense of the word can be claimed for this method, considerable prolongation of life with alleviation of symptoms has been obtained. Electro-coagulation, for instance, to the antrum, combined with radium placed directly in contact with the coagulated tissues has been productive of notable results, particularly in Stockholm, where this combined treatment was initiated by Dr. Elis Berven in collaboration with Dr. Gunnar Holmgren. It must be a matter of speculation as to the effect produced by combining radium with the destructive influence of heat or electro-coagulation.

The application of heat is visualized by most people as a process of ruthless and undiscriminating destruction and has thereby prejudiced the position against the use of such an agency. This is an unfounded belief. Experience and the concrete evidence of successful cases show that heat can be controlled and regulated in such a way as to render it an effective weapon.

Surgery, destruction by removal, still holds pride of place as a remedial agent. The scalpel is a means which is under more perfect control, can be estimated to a nicety, and can be used in proximity to great vessels and nerves in a manner that defies the capacity of other destructive agents. Its scope and application is so well known that further elaboration along these lines is unnecessary.

Knowledge of the natural history of the disease is essential before any assessment can be made of the relative merits of different forms of treatment, particularly where, in the disease under survey, the results obtained include so many cases in which palliation or prolongation of life without symptoms can alone be claimed. Particularly is this the case when, as so often happens, statistical data are based on the survival rate, no mention being made of the condition of health enjoyed by the patient, or the extent to which they are or are not free from the constitutional or local disabilities associated with the disease. Cancer is very variable; for instance, in its natural duration, whether considered in relation to individuals or in relation to sites. It occurs in a catastrophic fulminating form as in the following case:—

A married woman, aged 45, admitted May 3, 1932, with a history of having knocked the left breast ten weeks before; a lump, about the size of a hen's egg, appeared, and the skin became discoloured. There was no pain. On examination the left nipple was higher than the right. There was a hard mass in the left breast which was firmly fixed but was not painful. The skin over the whole breast was reddened and eczematous, with sloughing round the nipple. The supraclavicular and axillary glands were enlarged and firm. X-ray of chest showed no evidence of metastases. The patient died on June 23; the post-mortem showed the liver full of growth, secondary deposits in the pleura, and enlarged glands in the mediastinum and along the aorta.

A case may be cited of the opposite type, in which the patient was a young girl with an osteogenic sarcoma of the femur.

A young woman, aged 20, first seen in September, 1927. The history was that of an injury to the left knee two years previously, and a painless swelling just above the knee noticed for nine months. Her general condition was good. The local condition showed a hard nodular swelling on the lower end of the femur extending 6 inches up the bone. There were no enlarged glands. Amputation was refused. In March, 1929, walking became painful and difficult, and, as a result, the patient consented to the removal of the limb. Amputation was performed through the upper third of the thigh. The nature of the growth was verified by pathological examination. Previous cases of this type that have come under my care have developed secondary deposits in the lungs and thus rapidly proved fatal; that amputation was not strongly urged until the duration of the disease indicated that malignancy in this particular case was of an unusually low grade. I saw the girl some three months ago. She was in blooming health and full of energy.

In certain sites, cancer can be a very chronic lesion. Thus, Wyard, in his collection of breast cases, cites two cases which lasted over thirty years, in the rectal cases one of more than thirty years, one of over twenty years, and a third of nine years. But these, of course, are outstanding cases, and do not occur in such sites as the cervix, the tongue, the œsophagus or the stomach. In spite of such long-lived cases which weight heavily the statistics in favour of a longer life where they occur, it may be noted that only 10 per cent. of breast cases, 2 per cent. of rectal cases, 1·5 per cent. of cervix cases and 1 per cent. of tongue cases live more than six years.[7]

The period that may elapse before recurrence after surgical removal, which holding the field for so long, is still maintained as the criterion of comparison, is another factor in estimating the incidence of so-called cures. Thus, in my own experience, metastases have occurred 22 years after radical removal of a breast, 10 years after radical removal of a tongue and associated glandular areas, and a local recurrence has appeared 12 years after a radical hysterectomy.

That *radiotherapy* occupies at the present day a definite position in the armamentarium of the clinician who undertakes the care of patients afflicted with carcinoma there can be no doubt. The difficulty is to determine with any degree of exactitude to what extent radiotherapy rivals surgery or meets it on equal terms. Difference of opinion has been shown in an acute form, not only with regard to the clinical results to be obtained by mass radiation, but also as to the advisability of utilizing such a source for the purposes of clinical research. Radium in mass, it must be admitted, is a dangerous weapon, and it may be that the directors of radium policy in this country have acted wisely in so distributing the supply at their command as to ensure that as little harm as possible will result. Small quantities, too, may be dangerous if used in a manner which indicates a complete ignorance of the fundamental physical effects produced by radium in the tissues. I am able to illustrate a case of this kind:—

A man, aged 66, admitted May 10, 1932. History and previous treatment: Swelling noticed under tongue and in contact with the mandible in 1928. In July of that year the submaxillary glands were excised and radium needles were inserted into the growth. The main portion of the tumour persisted and a new growth developed on the outside of the mandible, between the gum and the lip. In November, 1929, radium needles were inserted into holes bored through the mandible from back to front. Present condition (when first seen on May 10): The tongue is bound down to the floor of the mouth at the sides; anteriorly it covers a deep sloughing crater. The gums have disappeared, and the mandible, from molar region on one side to molar region on the other, presents itself as a grey, foul, necrotic mass, in which can be seen the holes through which the radium needles had been inserted.

I conceive it almost impossible to derive from our English records any just and adequate estimate of the part that expert radiotherapy should take in the war against cancer. It is therefore advisable to refer to a table, elaborated by Professor Forssell, of Stockholm, from statistics based on cancer incidence throughout Sweden.[8]

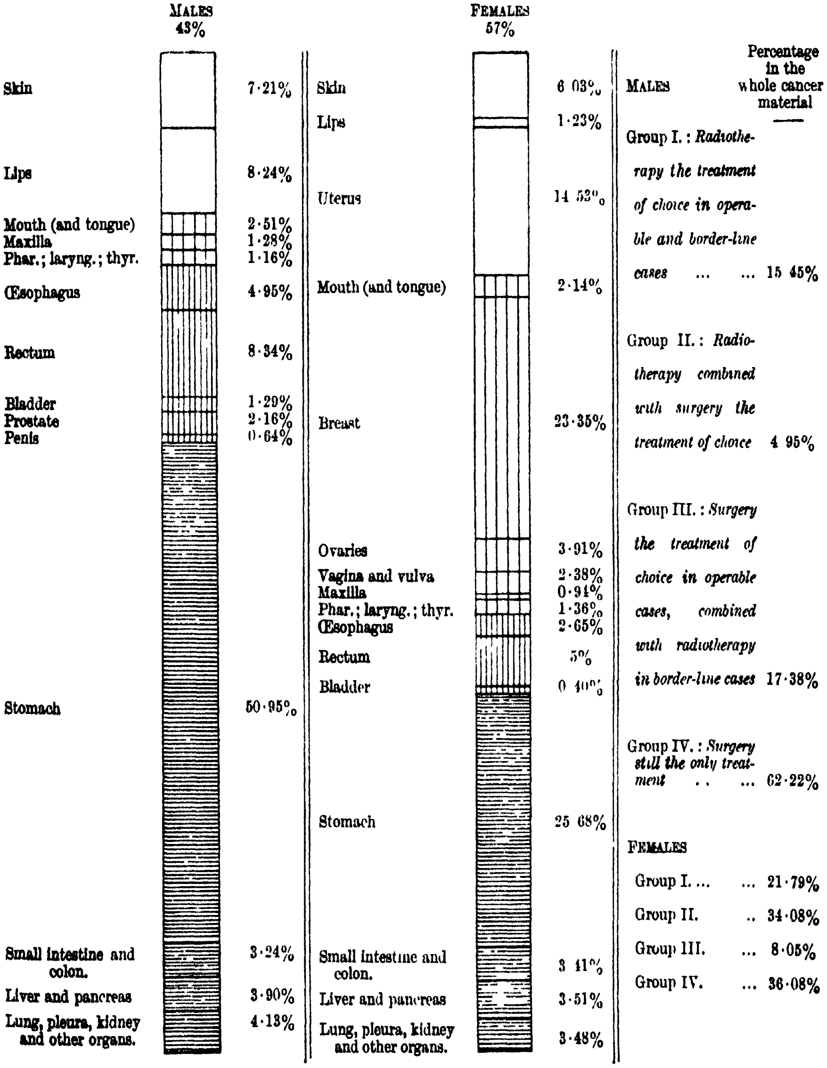
The table here shown indicates separately the incidence of cancer in various sites amongst males and females. It is to be noted that this table concerns carcinomas alone, the sarcomas being excluded. For the sake of convenience, the combined results, as set forth in this table, may be briefly summarized as follows :—Radiotherapy holds the field as the method of choice in carcinomatous lesions of the skin, lip

TABLE I.—(*Reproduced by kind permission of Professor Forssell.*)

DIAGRAM SHOWING THE SCOPE OF RADIOTHERAPY IN OPERABLE AND BORDER-LINE CASES

Estimated according to the results at Radiumhemmet and to the frequency of cancer in different parts of the body in the whole Swedish cancer material (Nyström's statistics). Males and females separately recorded.

Group I. ☐
Group II. ▥
Group III. ▥
Group IV. ▤



MALES 43%	
Skin	7·21%
Lips	8·24%
Mouth (and tongue)	2·51%
Maxilla	1·28%
Phar.; laryng.; thyr.	1·16%
Œsophagus	4·95%
Rectum	8·34%
Bladder	1·29%
Prostate	2·16%
Penis	0·64%
Stomach	50·95%
Small intestine and colon.	3·24%
Liver and pancreas	3·90%
Lung, pleura, kidney and other organs.	4·13%

FEMALES 57%	
Skin	6·03%
Lips	1·23%
Uterus	14·53%
Mouth (and tongue)	2·14%
Breast	23·35%
Ovaries	3·91%
Vagina and vulva	2·38%
Maxilla	0·94%
Phar.; laryng.; thyr.	1·36%
Œsophagus	2·65%
Rectum	5%
Bladder	0·40%
Stomach	25·68%
Small intestine and colon.	3·41%
Liver and pancreas	3·51%
Lung, pleura, kidney and other organs.	3·48%

MALES	Percentage in the whole cancer material
Group I.: *Radiotherapy the treatment of choice in operable and border-line cases*	15·45%
Group II.: *Radiotherapy combined with surgery the treatment of choice*	4·95%
Group III.: *Surgery the treatment of choice in operable cases, combined with radiotherapy in border-line cases*	17·38%
Group IV.: *Surgery still the only treatment*	62·22%
FEMALES	
Group I.	21·79%
Group II. ..	34·08%
Group III. ...	8·05%
Group IV. ...	36·08%

and uterus, constituting roughly 19 per cent. of all cancers in both sexes. Radiotherapy combined with surgery is regarded as the method of choice in lesions involving the mouth, maxilla, pharynx, larynx, thyroid, breast, ovary, vagina and vulva, constituting 19 per cent. of all cancers. Surgery alone is of use in operable cases, and combined with radiotherapy in border-line and inoperable cases of carcinoma of the œsophagus, rectum, bladder, prostate and penis, totalling 13 per cent. Finally, surgery alone can be expected to be of some value in 49 per cent. of all cancers, the lesions occurring in the stomach, intestines, liver, pancreas, kidneys and lungs.

Let it be admitted that the opinions expressed emanate from a man who has made radiotherapy his study in life; let it be admitted further that differences of opinion may exist on minor issues raised, and that the author will be prejudiced, if prejudice there be, in favour of the method which he has made particularly his own; taking all these things into consideration, the outstanding fact emerges that, were all these cases seen at a stage designated by the arbitrary term "operable," it is conceded that, in 81 per cent., treatment could not be accomplished without surgical collaboration and surgical aid. Professor Forssell, however, has pointed out to me that 60 per cent. of all cancer cases have, when first seen, attained a stage beyond the "operable" limit, and for about half these cases radiotherapy is a good palliative and can give freedom from symptoms in many cases. It must be remembered that the results indicated and the experience set forth emanate from a well-equipped radio-therapeutic clinic of more than twenty years' standing, staffed, moreover, by men whose ability may be gauged by their repute in the world of radiology.

For carcinoma of the intestinal tract radiotherapy has proved valueless, and that domain, therefore, belongs exclusively to the surgeon. The operative results associated with carcinoma of the stomach are, it must be admitted, disappointing; the small intestine is, for practical purposes, immune from the incidence of malignant disease; but it is in the colon and in the rectum that radical removal has attained its greatest triumphs.

A married woman, aged 49, admitted September 1, 1914, with a nine months' history of diarrhœa and passage of blood per rectum and aching pain. Examination *per rectum* revealed a hard, irregular ulcer on the posterior and left lateral walls which was freely movable. On September 29, 1914, an abdomino-perineal excision of the rectum was performed. This patient was seen a short time ago and was found to be symptom-free and leading a normal life.

That radiotherapy as a curative agent is preferable in many ways to surgical removal must be freely admitted, and for the following main reasons: The primary mortality is nil, whereas, according to the severity of the operation, primary mortality after surgical removal varies roughly from 5 to 20 per cent. Mutilation is avoided, thus eliminating cosmetic deformities and loss of function. This latter may be of such a degree that restoration must be undertaken by some plastic procedure, or it may constitute, as in the case of the tongue, an irreparable disability. The amazing way in which a fungating epithelioma of the lip, for instance, fades away under the influence of an adequate dosage of radium is little short of marvellous, and the reconstitution of the part to a condition practically normal in appearance and function is more marvellous still.

It may be asked then whether we are at present in sight of any means whereby the scope of radiotherapy as a sole and sufficient agency is likely to be increased. For the time being, and I say this with some timidity, we are at a standstill, and in the opinion of radiologists of repute our main hope of future progress depends on our ability to produce in the cancer cell a greater degree of sensitivity. It has been suggested that impregnation of the cancerous mass with heavy metals may tend to this consummation by the production, when irradiated, of secondary radiations, and so to the determination of a localized intensive effect which is beyond our power with the means at present at our disposal. Experiments on these lines have recently been conducted in the research and physics departments of the Cancer Hospital, but it has unfortunately to be reported that the work of Mayneord and Burrows[9] gives little hope that any results of note are to be obtained by the introduction of heavy metals, either locally, or by the intravenous route.

When it is remembered that surgery is useless, although indicated, in inoperable cases, when it is further remembered that in those cases in the treatment of which radium or X-rays holds pride of place, the prognosis depends upon the localization and extent of the disease in terms of operability, we are able to formulate an urgent plea, not only for earlier diagnosis, a subject which touches us in our professional capacity, but a plea to the public that they, in their own interests, shall co-operate with us, in submitting to us for our opinion, any departure from the normal which may have a cancerous or a pre-cancerous significance.

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ACUTE POLIOMYELITIS

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ACUTE poliomyelitis appears to be a disease of comparatively recent introduction. It is, of course, possible that it has existed at all times and has only been recognized as a separate entity recently, but one feels that a disease with such clear-cut features, especially when appearing in epidemic form, would be certain to have found a niche in medical literature. Sir Walter Scott, for instance, suffered from infantile paralysis at the age of eighteen months, and has left a striking description of the features of the disease. He was attended by some of the most observant physicians of the day, and they were quite unfamiliar with the condition. This fact in itself is a fairly certain guarantee that poliomyelitis was rare in this country at that time.

In this, as in all countries, poliomyelitis occurs sporadically. Often only one case occurs at a time in a given district, while more frequently a minor epidemic of two or three cases occurs in a village in the course of a year, and thereafter no more cases are seen for several years. These sporadic cases are relatively commoner in small industrial towns and in the country districts than in the large cities. In the south-east of Scotland, for instance, the mining villages and country towns are responsible for a large proportion of the annual cases.

Super-added upon these sporadic cases, large epidemics are liable to occur, varying from the small outbreaks of some twenty cases which we have hitherto had in this country up to the enormous outbursts of the disease with which Northern Europe, and especially America, have been afflicted. Starting in Scandinavia, epidemic forms of the disease have appeared throughout the world. America suffered from an outbreak of 139 cases in 1894, and this was succeeded between 1907 and 1910 by an enormous epidemic during which it is estimated that something like 15,000 cases occurred per year. In 1916 another very large outbreak occurred in New York and spread to other States. Nevada, New Mexico, Georgia and California were the only ones to escape. This epidemic followed what is known to be the usual rule by starting during the hot weather in June. It commenced in Brooklyn and spread over New York by contact. In addition, fresh foci of the disease soon appeared by, as it were, metastasis, along all lines of communication to other centres, such as Boston, Baltimore, Philadelphia and Chicago. During the latter six months of 1916 alone, 13,000 cases occurred.

In all countries it has been found that a period of sporadic incidence has been followed by a gradual increase in the disease which has been the prelude to the outbreak of an epidemic. So far, in this country, we have suffered from one or two very minor epidemics, but there cannot be any doubt that the number of sporadic cases is slowly rising and that we stand on the verge of a serious epidemic at any time. It is, therefore, of the greatest importance that a knowledge of the main features in the pathology and treatment of the disease should be diffused as widely as possible.

Cases may be divided into those typical ones which exhibit flaccid paralysis and which are self-evident when the paralysis appears, and the abortive cases exhibiting the pre-paralytic symptoms, but never developing paralysis. These abortive cases are, however, capable of spreading the disease, and may possibly develop into carriers. When dealing with the sporadic type of the disease, it is found that it affects mainly children under five years of age, that the mortality is low, and that abortive cases either do not occur or, what is much more likely, are not diagnosed. During epidemics, on the other hand, adults are frequently affected as well as children, the mortality may rise to considerable heights, and it becomes possible to make an intelligent effort at the diagnosis of abortive cases and of ordinary cases in the preparalytic stage.

Infantile paralysis has been proved to be an infectious fever and to belong to the class of virus diseases. Occasionally in practice one comes across definite evidence of contact infection in sporadic cases, but such case-to-case infection is only frequent during epidemics. In 1909, Landsteiner and Popper in Germany showed that an emulsion of the spinal cord from a case during the acute stage of the disease would reproduce the disease when injected into monkeys. Various organisms were suggested as the cause of the disease; but inside one year five independent sets of investigators in France, Germany, Austria and America showed that we were dealing with a filterable virus which passes through a Berkefeld filter and is very difficult to destroy. Flexner and Amoss, for instance, have reproduced the disease from a virus which had been preserved in glycerin for six years.

It is generally accepted that the virus is carried to the naso-pharynx by droplet infection from a person incubating the disease, or from a carrier. It is clear that the carrier rate is at the moment low, or that the children of the population are at present largely immune to the disease. When the carrier rate rises or the immunity falls, an epidemic is due. The virus may be reclaimed from the nasal mucosa or even from nasal washings after death in fatal cases. From the nasal mucosa the virus probably extends along the sheath of the olfactory nerve filaments by the perineural lymphatic spaces which communicate with the subarachnoid space. By this means the cerebrospinal fluid becomes infected. The infection of the naso-pharynx sometimes causes a mild nasal catarrh or sore throat at the commencement of the disease. The presence of the virus in the cerebro-spinal space causes the next symptoms, namely, fever, malaise, and pain in the back as the result of a degree of meningeal reaction.

The virus now extends into the central nervous system along the perivascular spaces which are prolonged along the cortical cerebral and spinal vessels. The possibility of absorption of lampblack along this route has been demonstrated experimentally, and the progress of the virus is marked out histologically by a column of œdema and inflammatory reaction. The fact that infection normally takes place by this route is backed up by the finding that monkeys are more easily infected by painting the virus on the nasal mucosa than even by its intravenous injection. It is, curiously enough, difficult to demonstrate the virus in the cerebro-spinal fluid. Flexner found that it could only be reclaimed upon the third day before paralysis occurs. It has also been found that the incubation period of the disease in the experimentally infected monkey varies from three to thirty days, but is usually about nine days. There are no reliable data upon which to base an estimate of the incubation period in the human being.

The subsequent changes in the central nervous system consist of a marked inflammatory reaction and accompanying œdema which affects mainly the anterior horn of the cord. The presence of the œdema compresses the motor nerve cells in the anterior horn, causing paralysis. When the œdema decreases, the compressed cell may recover, but, if it has been devitalized, it is replaced by overgrowth of neuroglia. Small hæmorrhages frequently accompany the œdema, and the process, though commonest in the cord, may affect any portion of the central nervous system.

The pressure paralysis of the motor cells in the anterior horn causes a flaccid paralysis of the muscle fibres supplied by the affected cells. A similar œdema of the posterior nerve root and sensory ganglion is often found, and is probably responsible for the well-known muscular pain which is met with in the acute stages of the disease. In cases of widespread and persistent paralysis, vasomotor and trophic disturbances may be found in the affected limb.

When the acute œdema of the cord diminishes, some motor cells will recover their function and muscular power will return; while others, which have been completely destroyed, will never recover, thus leading to a greater or less degree of permanent loss of muscular power.

The recovery of power in the case of a motor cell which has been temporarily paralysed will depend upon two factors: (1) The cessation of pressure from œdema. (2) The condition of the paralysed muscle when nervous impulses reach it once more.

(1) It has been shown, and it is obvious that it must be so, that any activity in the central nervous system is accompanied by vaso-dilatation. Every movement of a limb, every sensory stimulation of a limb, is reflected in the corresponding area of the cord by an area of vaso-dilatation. It is obvious that our first duty, having regard to the amount of œdema already present in the cord, is to refrain, by all means at our disposal, from adding to this œdema by stimulation of the tender and paralysed limb until such time as the inflammatory process in the cord is no longer active. The first principle in the treatment of the acute stage of poliomyelitis is, therefore, to provide for complete immobilization and rest for the paralysed muscles, and to avoid stimulation by massage or any other means until the acute stage is past. This usually means for a period of several weeks until all general illness and all muscular tenderness have gone. It is clear that this splinting must be carried out most carefully in

order to avoid pressure sores. It is necessary to insist upon the great importance of adequate orthopædic treatment during this acute stage. It may be said that, though infantile paralysis may be looked upon as a disease which is likely to come under the observation of the physician during the pre-paralytic stage, from the moment paralysis appears, or even as soon as a diagnosis is made, should it be arrived at before paralysis develops, the disease immediately becomes an orthopædic one. In the past much easily avoidable paralysis has undoubtedly been caused by neglect of skilled orthopædic treatment during the acute stage. One day of adequate splinting at this stage is worth months of patient work at a later date.

(2) The paralysed limbs must be splinted in such a position that they will easily recover their function when the motor cells recover. All paralysed muscles must be kept relaxed. In the case of a completely flaccid limb, the joints are splinted in positions which will relax those muscles which we know from experience are slow to recover. Thus the legs are splinted in abduction, in order to relax that most important of pelvic muscles, the gluteus medius. The knees are fixed in a slight degree of flexion, and the ankle joints with the feet at right angles to the leg. In the case of the upper extremity, the deltoid muscle, and especially the posterior fibres of that muscle, are a frequent cause of trouble, and the arm is splinted in right-angle abduction and external rotation at the shoulder joint. The elbow is fixed in right-angle flexion, the forearm in supination, and the wrist in dorsi-flexion. When recovery commences, the appearance of muscular power in various muscle groups is carefully followed and the position of the limb altered to suit the process, always keeping the weaker muscles relaxed. Paralysis of the para-vertebral muscles is treated upon similar lines, the muscles being relaxed by placing the patient upon a spinal frame of the Whitman type, with the vertebral

column hyper-extended. The process of splinting described will, of course, prevent the development of deformities from unbalanced muscle action in a partially recovered limb.

Muscle atrophy starts within a few weeks of the onset of the paralysis. If the muscle does not recover power, the atrophied fibres gradually disappear, and the muscle is converted into a thin strand of connective tissue representing the original fibrous skeleton of the muscle, with a good deal of fat in it. Sometimes a fatty enlargement of the paralysed muscle takes place. In old standing cases, the blood supply to the limb may be so poor that gross shortening takes place.

Six quite definite types of poliomyelitis may be recognized: (1) The *spinal* type, which is the common variety. (2) The *meningeal* type, where a marked meningeal reaction takes place in the early stages, and which is therefore commonly mistaken for meningitis. (3) The *progressive ascending* type. This accounts for many of the fatal cases, the paralysis starting in the cord and mounting higher and higher until the respiratory centres are paralysed. (4) The *bulbar* type, affecting the brain stem. In this case there may be paralysis of cranial nerves. (5) *Polio-encephalitis*, giving rise to spastic forms of paralysis when the motor centres are affected and being followed frequently by mental changes. (6) The *ataxic* case. Occasionally, an attack of poliomyelitis is followed by ataxia of the type met with in tabes dorsalis, apparently as a result of destruction of the cells of the sensory root ganglia.

DIAGNOSIS

The diagnosis of the common spinal type does not present many difficulties when paralysis has appeared. It is with the diagnosis in the pre-paralytic stage and of abortive cases with which we have to deal. Diagnosis in the absence of paralysis is only a working possibility in the presence of a large number of cases such as might be found during a large epidemic. There is no definite symptom-complex which will make diagnosis in the pre-paralytic stage anything more than an intelligent guess. A vague and otherwise inexplicable febrile illness, especially if it be accompanied by a slight nasal catarrh or sore throat followed by slight symptoms of meningism, in the form of headache and a little pain in the back, will invariably be attributed to a cold, influenza or teething. In the presence of an epidemic of poliomyelitis, however, the practitioner will not do his duty by such a patient unless he looks upon the case as one of poliomyelitis until events prove him wrong. If such a suspicion of an abortive or pre-paralytic case arises, a lumbar puncture should be carried out.

The cerebro-spinal fluid is usually increased in tension but clear in colour. There is an increase in protein, and also an increase in cells of the lymphocyte variety. Occasionally, there is a trace of blood present. "Froin's syndrome" of rapid coagulation is sometimes seen. If the fluid be shaken up in a test-tube, the froth which forms tends to persist for more than half an hour. The fluid reduces Fehling's solution in most cases, and this fact often enables a differential diagnosis to be made from meningitis. Bacteriological examination is, of course, negative.

TREATMENT

Poliomyelitis may be divided into the following stages. The stage of incubation, in which symptoms are absent, a diagnosis cannot be made and no treatment can, of course, be advised. This is followed by the stage of invasion, or the pre-paralytic stage, manifesting itself by the vague symptoms alluded to above. In many cases, these symptoms will be so slight that the practitioner will not see the case during this stage. In some cases during the course of an epidemic, an intelligent diagnosis may be arrived at. We next have the acute or paralytic stage of the illness manifested by flaccid paralysis, pain and tenderness of the affected limbs and a greater or less degree of fever. This is followed by the stage of recovery, which is rapid for a few months only, but which may be prolonged for as much as two years, and this in turn succeeded by a stage of residual paralysis.

The stage of invasion.—It has been shown that one attack of poliomyelitis confers immunity upon the individual for the rest of his life. It has also been shown that the serum of a person who has at any time suffered from the disease is capable of aborting the disease and preventing the onset of paralysis in monkeys if administered during the pre-paralytic stage. Clinically, this immune serum has been widely used to abort the disease. The results are impossible to estimate, as the diagnosis arrived at in the pre-paralytic stage is so uncertain. In view of the experimental findings, however, the administration of immune serum would appear to be definitely indicated in the stage of invasion. In cases where such immune convalescent serum is not available, it has been shown that serum from a healthy adult is likely to be nearly as efficacious. Most adults are immune to the disease, and a small blood transfusion in the pre-paralytic stage is more likely to be of benefit than not, and can in any case do no harm. Apart from such serum therapy, rest is indicated during this stage.

The acute or paralytic stage.—When paralysis has appeared, we have seen that it is of vital importance that absolute rest to the paralysed muscles be secured by skilled splinting in the ideal positions at the very earliest possible moment. Serum has been used during this stage in the hope that it might limit the spread of paralysis, but its action is very difficult to evaluate.

The stage of recovery.—During this stage, the œdema of the cord having passed off, the paralysed muscles must still be kept relaxed by splinting, and the position of the limbs altered from time to time in order to keep the weakest muscles more relaxed than those which are partially recovered. The development of deformity from unbalanced muscle action is prevented by the same means. At the same time, we are now at liberty to do all in our power to preserve the nutrition of the paralysed muscles by massage and heliotherapy. Finally, re-education of the recovering muscles by carefully graduated and assisted exercises at the hands of a skilled re-educational masseuse now becomes of the greatest importance. The treatment of this stage must be continued for two years before the remaining paralysis can be said to be permanent.

The stage of residual paralysis.—The first measure of treatment in a case in this stage is the correction of deformity if this be present. In a properly and patiently treated case no deformities should have been allowed to arise. If, however, they are present, they must be corrected. It will then be found that a noticeable return of muscular power may occur as a result of the relaxation of the stretched muscles.

Permanent muscular weakness is treated by patient muscular re-education to train to the fullest extent every available shred of muscular tissue which may be present. Various operative measures may be utilized during this stage in order to stabilize flail joints, by arthrodesis of the knee or shoulder, Dunn's arthrodesis of the subtaloid and tarsal joints, or astragelectomy. Where the return of power is good, a weakened group of muscles may be strengthened by tendon transplantation from a stronger group. By such measures it is usually possible, in all but the most widespread cases, to produce, if not a normal individual, at all events a person who is capable of walking and of taking his or her place in life without becoming a burden upon the State.

THE CIRCULATORY FAILURE IN DIPHTHERIA AND ITS TREATMENT

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IT has long been recognized that diphtheria is attended by a profound toxæmia, and that from the commencement of the disease there is a progressive fall in the systolic and diastolic blood-pressures. Many variations in the dosage of diphtheria antitoxin have been advised, and recently it has been shown that in many cases very large doses are not called for. I shall attempt to show that there is a direct relation between the antitoxin and the blood pressure which makes even more careful dosage necessary. We are indebted to Esther Harding[1] for her work on circulatory failure in diphtheria, and to J. D. Rolleston[2] for suggesting a method of overcoming this failure by vaso-constrictors.

The diphtheria bacillus can be readily grown outside the body in suitable media, and while little is known of the chemical composition of the toxin, its effects on animals can easily be seen by its inoculation. If the toxin be injected into a guinea-pig, the same clinical picture is produced as in a guinea-pig inoculated with diphtheria bacilli, which proves that it is the toxin which produces the effect and not the diphtheria bacilli *per se.* If a guinea-pig is inoculated with a lethal dose of toxin and this is immediately followed by a sufficient dose of antitoxin the animal is quite unaffected. If, however, a period of two to three hours is allowed to intervene, the animal will certainly be profoundly affected by the toxin and may die, proving that the toxin almost immediately unites with the tissues, the importance of this fact will be evident when we come to the treatment of diphtheria with antitoxin.

The circulation of the blood is dependent on three factors, namely, (1) the force of the heart, (2) the tone and elasticity of the blood vessels—which also includes vaso-constriction and vaso-dilatation, and (3) the volume of the blood; and it is necessary for us to have an understanding of the working of these three factors in health so that we can comprehend how they become affected during an attack of diphtheria.

The pathological changes in diphtheria have been fully investigated by several workers ; and in nearly all cases fatty degeneration has been observed, and, after the fourth day, myocardial degeneration can be seen in all severe cases; there is a leucocytic infiltration of the muscle, vacuolation, and splitting of the nuclei, the muscle tissue becomes very friable and toxic, and in a certain proportion of cases there is an associated endocarditis. The vessels lose their tone owing to degenerative changes taking place in the muscle tissue, and there is proliferation of the intima. The nervous system also shares in the degenerative changes; hyaline degeneration begins in the myelin sheaths, and the axis cylinders show irregular swellings.[4] The cerebrum, medulla, anterior and posterior roots also show like degenerative changes.

The first clinical evidence usually commences in the throat. The fauces are at first red and inflamed and small white spots appear on the tonsils; the exudate next appears and rapidly spreads over the tonsils in direct relation to the virulence of the infection, and, within reasonable limits, the greater the spread of the exudate, the greater the amount of toxin that will be absorbed into the system. At this stage the toxæmia begins to make itself manifest by a growing disinclination of the patient to move, general malaise and nausea. There is marked pallor of the skin, which will be referred to again; the pulse becomes more rapid, and the first heart-sound is weakened in its intensity; the fever is early and rapidly subsides, anything above 103° F. being unusual; the urine is scanty and in many cases contains albumen. The circulatory system is profoundly affected in diphtheria, and when death takes place during the first ten days it is almost always due to circulatory failure. In all the cases that I have treated, I have taken the blood pressure at regular intervals, in most cases twice or thrice daily. During the first two days when the throat is just beginning to show exudation, the blood pressure remains normal; it then begins to fall both in systolic and diastolic periods, the systolic pressure falling at a greater rate than the diastolic, so that the pulse pressure becomes less and, where death occurs, the systolic and diastolic findings become almost the same. In those cases which end in recovery the blood pressure very slowly regains its normal level, and even at the end of six weeks it is considerably below normal. This is partly due to the fact that when the blood pressure is first taken the patient is usually in a somewhat excited condition of expectancy, with the result that erroneous pressures are read, and in part due to the fact that the continued rest in bed and lack of exercise have a lowering effect on the blood pressure.

The fall in blood pressure is caused in several ways, and if we remember that there are the above three factors responsible for keeping up the blood pressure, it is obvious that it is these that diphtheria attacks. First, we know that the heart wall is affected with degenerative changes, that the first heart sound is diminished on auscultation, and that the pulse rate increases, which are all signs of diminished output of blood from the heart, and consequent fall in blood pressure. From the pathological findings[5] it appears that in diphtheria the heart is the first to suffer, and this is amply corroborated by the fact that it is the systolic pressure which first falls, for it is the systolic pressure which is the criterion of the force of the heart, and the diastolic pressure which registers the condition of the arterial system. Secondly, we find that the diastolic pressure begins to fall, which shows that changes are taking place in the systemic circulation as well as in the heart; this is due to several factors, each in its part contributing towards the paralysis of the circulatory system. The musculature of the vessels shares in the general toxæmia in the same way as the heart; the weakened musculature means lack of tone, so that if the pressor impulses remain constant there will not be the same degree of vaso-constriction as would naturally be expected, if the normal tone was present; this gives rise to a larger total area in the calibre of the vessels with the same quantity of blood and of necessity lowers both diastolic and systolic pressures. Thirdly, it has been shown that cold produces paralysis of the pressor afferent fibres before the depressor become affected, and, similarly in the case of diphtheritic toxæmia, it is only reasonable to suppose that fatty degeneration will first make its appearance in those nerves which are most easily destroyed.[3] It will be immediately manifest that, if pressor impulses cannot reach the centre of vaso-constriction as easily as the depressor, there will be vaso-dilatation and consequent lowering of blood pressure. It will be realized from the above statement that not only is the blood pressure a reliable indication of the patient's condition, but is of great assistance in making a prognosis.

It is almost impossible to make an accurate prognosis in any case of diphtheria, as even the most simple case may suddenly die from cardiac failure, or paralysis, but I have found that the blood pressure forms the best guide as to the patent's condition. If the blood pressure remains about the same level, the prognosis is good; if, however, the fall is rapid, particularly in the diastolic pressure, this is of bad portent. The first heart-sound usually becomes muffled about forty-eight hours after the lowering of the diastolic pressure.

Antitoxin treatment is, of course, the most important and effective mode of treatment in all cases, but unfortunately if used indiscriminately it can do quite as much harm as good. A large dose given intravenously to a patient *in extremis* is almost always fatal. I found that the antitoxin also caused a drop in the blood pressure,[4] and if a person who is not suffering from diphtheria be given 12,000 units the blood pressure begins to fall twenty-four hours later; this fall usually lasts about three days when the blood pressure quickly becomes normal again. The drop is not usually more than ten millimetres, and the diastolic pressure is not so much affected as the systolic. It is clear that if a person *in extremis* with a systolic blood pressure of 50 mm. is exposed to a further drop in the blood pressure from the administration of antitoxin, death is likely to follow. I have also noticed that the fall in blood pressure is more pronounced and rapid in onset if the antitoxin be given intravenously rather than intramuscularly, and that 12,000 units very rarely causes a fall of more than ten mm. Hg. The cases that I have treated recently have not been given more than 12,000 units, and the dose has not been repeated unless the patient's condition makes it necessary, and the blood pressure is not falling rapidly. The earlier the antitoxin is given the less is its effect on the blood pressure, so that suspected cases, and those coming under treatment in the first two days, should be given about 24,000 units. In all severe cases of diphtheria, even if they be hæmorrhagic, no more than

12,000 units should be used, and this dose should not be repeated unless the blood pressure is not falling, and that is a condition which is not often present. The antitoxin should always be administered intramuscularly so that there shall be a minimum of lowering of the blood pressure.

The general measures that should be taken include rest, absolute, the patient remaining prone without pillows, and under no circumstances should he be allowed to sit up to take food or for any other reason. He should be given an enema at regular intervals. In respect of diet: during the first week he should have a bland fluid diet, which should include such articles as beef extract, Brand's essence of chicken, calves' feet jelly, Benger's food. However, in all severe cardiac cases it is better to commence treatment with a nutrient enema. The patient is best kept quite prone until the blood pressure has stopped falling when he may be allowed a pillow a week to bring him gradually into a sitting posture, and the diet may be increased. It is most important to keep the patient warm and quiet, and all visitors should be excluded.

Medicinally, many drugs have been tried but very few have shown themselves to be of any use whatever. Until quite recently no specific drugs had been advocated, and it was not until J. D. Rolleston advised giving doses of adrenaline to patients *in extremis* that there has been any hope of anything specific being found. I have tried adrenaline and found that the blood pressure was somewhat raised and that the patient became a little better for a while, but very soon sank back into his original condition. The failure of the adrenaline is due to its particularly rapid and unsustained action, and I now use ephedrine in all cases of diphtheria, for its action is prolonged and it can be repeated, while if it is given to a patient who has not got diphtheria it causes a rise in blood pressure but does no harm of any sort whatever. I now give all cases ephedrine from the moment they come under treatment, and I find that the blood pressure does not drop so quickly or so much, the patient does not present so much pallor, and more antitoxin can be given than if ephedrine has not been administered. The ephedrine should be given every six hours, and in maximum doses according to age. Ephedrine is very effective as long as the patient's condition does not become too bad, but then it appears to lose its effect. If this state is reached the patient should receive, as well as the ephedrine, a maximum dose of pitressin, which is the blood-raising element of pituitary, and it should be given at six-hourly intervals until the patient's condition warrants its cessation. The effect of the pituitary extract is absolutely specific in diphtheria, and if it be given to an apparently almost dead patient he will often rally for some considerable time. I give with the pituitary intramuscularly 2 c.cm. of hexeton or camphor in oil, which seems to aid the action of the heart, and the end of the bed is raised, the patient kept very warm, and a light linseed meal poultice put over the heart, preferably with mustard (1 to 6 parts). If the patient is not vomiting the following mixture is of use :—

℞	Spt. aetheris	ʒiiss
	Spt. chloroformi	ʒi
	Spt. ammon. aromat.	ʒiii
	Aq. ad	℥vi

Sig. One tablespoonful in water, every four hours.

Strychnine, digitalis and belladonna seem of little or no use, and I am certain that in the case of strychnine its action is impaired by the existing damage to the nervous system, as it will be noticed that all the above drugs (ephedrine, adrenaline, and pituitary extract), do not act via the damaged nervous system, but on the nerve endings or on the muscle direct. Oxygen does not seem to be of much use in averting a fatal issue, but it should certainly be used if there is any sign of cyanosis. With regard to alcohol, I think that all severe cases should receive brandy or alcohol in some form or other, in maximum nutritional doses. In the case of children it is usually administered as white wine whey, which, if carefully prepared, is easily taken.

We may conclude, then, that the circulatory failure in diphtheria is due to vaso-dilatation, weakened cardiac output from the action of the toxin on the heart muscle, and damage to the arterial wall, and that, provided that the antitoxin be given early enough, the blood pressure would not fall sufficiently to cause any serious circulatory failure; but should the antitoxin be given late for any reason, or should the blood pressure fall from any of the previously considered factors then the only really effective treatment is in giving vaso-constrictors.

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TREATMENT OF PARESIS OF THE BLADDER BY RESECTION OF THE PRESACRAL NERVE

By HAMILTON BAILEY, F.R.C.S.

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EXCISION of the presacral nerve provides a method of increasing the emptying power of the bladder, and should prove useful in the difficult group of cases in which there is partial paralysis of the bladder without mechanical obstruction. The operation has the advantage of safety, and can be performed swiftly and without shock, indeed, presacral neurectomy is considerably less dangerous than repeated catheterization.

The rationale.—Learmonth's writings make it quite clear how the bladder's power of contractibility improves after presacral neurectomy. The involuntary musculature of the organ is controlled by two antagonistic nervous mechanisms, the parasympathetic and the sympathetic. The *parasympathetic nerves* come from the 2nd, 3rd and 4th sacral nerves and their fibres pass straight through the hypogastric ganglia (Fig. 1) to reach the bladder wall. These nerves are the motor nerves of the muscle strands, and inhibit the involuntary sphincter. In other words, they are the *emptying nerves* of the bladder. The *sympathetic nerves* have wide connections which just below the bifurcation of the aorta collect into a nerve trunk—the presacral nerve. Typically this nerve trunk, after running downwards in the middle line in front of the sacral promontory, bifurcates, each limb passing to the vesical musculature. The action of the sympathetic nerves on the bladder musculature is diametrically opposite to that of the parasympathetics;

in other words, these nerves are the *filling nerves* of the bladder.

If the parasympathetic nerves, the emptying nerves of the bladder, are acting feebly, the sympathetic, the filling nerves, will overact, and retention results. The rational line of treatment in such a case is to throw out of action the filling nerves, when the feebly-acting emptying nerves will function sufficiently to allow the contents of the bladder to be expelled.

In the following case this principle was applied with a dramatic result. The presacral nerve was carefully dissected and the area depicted in black in Fig. 1 was removed.

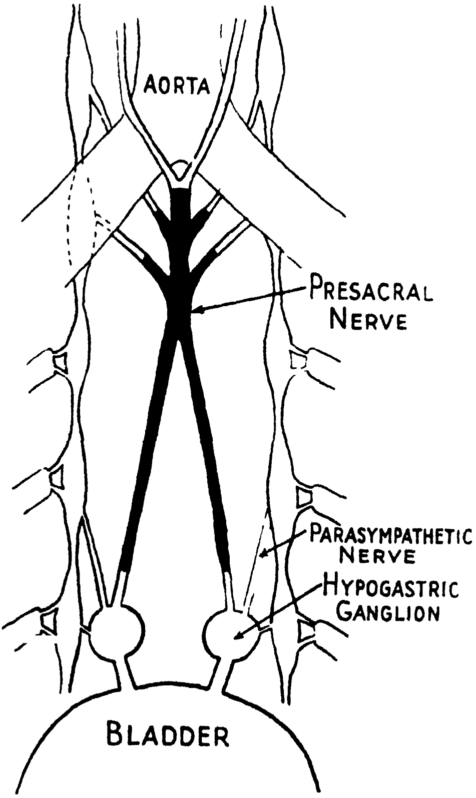

FIG. 1.—Diagram of the innervation of the bladder. The portion depicted in black was excised in the case described in the text.

Following Cæsarean section in the spring of 1932, a married woman, aged 30, experienced intractable urinary retention, which did not respond in the slightest degree to any of the usual remedies. No cause could be found for the retention, and after repeated catheterization attacks of acute and subacute pyelonephritis supervened. When the infection had abated, it was considered advisable to explore the abdomen, as the possibility of perivesical adhesions following the Cæsarean section appeared to be the only explanation of the trouble. Laparotomy was performed by Mr. F. W. Roques, who found many adhesions in the pelvis tethering the uterus. All the adhesions were freed and a subtotal hysterectomy performed. She made a smooth recovery from the operation, but the urinary retention persisted. A course of electrical treatment and later suggestion combined with strychnine did not bring about the slightest improvement, and the notes state there was seldom less than 20 oz. of residual urine in the bladder. On January 13, 1933, I reopened the abdomen; there was hardly an adhesion to be found and I at once proceeded to remove the presacral nerve, a measure which in this case presented no difficulty. On the next day the patient completely emptied her bladder naturally, and has continued to do so up to the present time. Her general condition has greatly improved. Investigation shows that whereas before presacral neurectomy there was between 20 and 30 oz. of residual urine there is now not more than 1 oz.

There is every reason to believe that bladder function has been restored permanently, but even if this rosy prognostication is inaccurate this case demonstrates conclusively that the theory of the method is sound.

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A NOTE ON THE USES OF GLUCOSE IN GENERAL PRACTICE

By F. O. TAYLOR, M.B., Ch.B.

THE general practitioner who has attended many families for some years knows from experience which of his young patients are prone to develop acidosis. As a rule they are of the nervous and delicate type, and readily go under to catarrhal infections. For some years, on the ground that alkali neutralizes acid, I tried to saturate these children's systems with bicarbonate of sodium, magnesium carbonate, and the like. But often vomiting was caused or increased; the temperature remained high, the breath fruity ; these symptoms show that, although there is not any demonstrable complication, the parents should be warned that some serious condition may be on the way. By slow stages, however, recovery would come, no doubt assisted to some extent by persistent alkaline medication. In passing, let me say that ammonium acetate has kept a high place in the purely medicinal treatment of juvenile sufferers from feverish complaints.

About eight years ago, after worrying for several days about the apparently serious condition of a child of 3 years of age who was maintaining a temperature of 102–104° F., without any obvious cause and with acidosis for which the usual alkaline treatment was given, I remembered that glucose was stated to be of value in such cases and promptly prescribed it. The temperature fell at once, and the child improved in an extraordinary way. Since then a load has been taken off my mind. If the acidosis is relieved but feverish malaise still persists, there must be some further complication.

Recently I attended a boy of 8 years with obvious acidosis. The administration of two heaped teaspoonfuls of medicinal glucose every two hours in water stopped his vomiting, cleared his urine, and removed the fruity odour from his breath, but did not bring down his temperature or stop some vague pain in the left upper epigastrium. I expected further developments. Eventually a basal pleurisy appeared.

Another small patient, always easy to treat for his chills and colds, one day did not respond to the usual measures; as a matter of fact he became seriously ill with only very vague abdominal pain. I sent the boy to hospital, where also he was treated as an obstinate case of acidosis : operation later revealed pneumococcal peritonitis.

Negative observations are as useful in some cases as positive findings. Glucose cannot *cure* bacterial infections. As children grow, so does their liability to acidosis diminish. The adult simulates the condition with hyperacid urine and gastric secretion. But the fruity breath, in my experience, is usually associated with the acetonuria of diabetes, or with the terminal stages of dissolution.

As a valuable food, non-irritating, and easily absorbed, glucose is the only nutriment which I allow to adults during the rare cases of pneumonia I see nowadays. In hyperemesis gravidarum it can be freely used as a rectal meal with or without normal saline, and asthmatic children often derive great benefit from large quantities in addition to ordinary diet.

PRACTICAL NOTES

PRACTICAL HINTS FROM GENERAL PRACTITIONERS

Much useful information on diagnosis, prognosis, and more particularly treatment is accumulated by those in general practice in the course of years, but never comes before the medical profession. Contributions of this type to the pages of THE PRACTITIONER *are therefore especially invited from readers in general practice. Such notes will be included in a special section of this journal, and should be addressed to the Editor,* THE PRACTITIONER, *6–8 Bouverie Street, London, E.C.4. The notes should be short, in any case not exceeding 500 words, and should embody practical hints and prescriptions useful to general practitioners.*

Anæsthesia from the General Practitioner's Point of View

Mark C. Lidwell (*Medical Journal of Australia*, December 24, 1932, 11, 767) is of opinion that ethylene has been the biggest advance in anæsthetics in recent years, but there are certain things which will eliminate its use in general practice: (1) danger of explosion; (2) the weight of anæsthetic machines to be carried about; (3) lack of skill by the man who is not using it every day; (4) the cost of apparatus and gases. Ether has been a well-tried servant and it has very seldom let one down. It may not be nice to take, but, if preceded by ethyl chloride, it is not at all unpleasant. If glucose and orange juice be given an hour or two before the operation, post-operative vomiting will be reduced to a minimum, especially if the ether is being administered by means of a machine. Ether is safe, portable and cheap, and has stood the test of time. Avertin and sodium amytal are excellent basal anæsthetics, but must be measured carefully and not in a haphazard manner, and should never be used, except under exceptional circumstances, for full narcotization.

The Uses of Regional Anæsthesia

No matter what be the practice of Continental surgeons, in this country general anæsthesia, when practicable, remains the procedure of choice. Daniel Lamont (*Glasgow Medical Journal*, October 1932, cxviii, 233) insists at the same time it must be clearly understood that the skilled employment of regional anæsthesia can permit of the performance of any surgical operation with safety to life, so far as the anæsthesia is concerned. In general terms it can be said that the method is indicated in minor surgery, in chronic disease of kidneys, lungs and circulatory system; in septicæmia, shock, hæmorrhage, obstructive jaundice and cachetic states. Also it is a substitute for general anæsthesia in neck operations, particularly goitre and tracheotomy. The method, in the main, is not suitable for babies or very young children. As regards post-operative complications, regional anæsthesia does not abolish the ever-present risk of pulmonary embolism, but it eliminates the opportunity for pulmonary complications by the irritation of air passages. Vomiting, flatulence and strain are abolished and normal diet is not interrupted, provided the nature of the particular operation permits of its continuance. It is not a fact that post-operative pain is more severe after this form of anæsthesia. Regional anæsthesia can be invaluable to the surgeon or practitioner working single-handed, say, in remote country districts. Regional anæsthesia can be effected in two ways : (1) by *field block*—where a barrier of solution is injected around the area at some distance from it. For example, a sebaceous cyst of the scale can be painlessly removed after a diamond-shaped barrier of solution has been injected around it and about 2 inches or so away from it. This is a simple procedure. Only the subcutaneous tissues require blocking. In the abdomen, in addition, the deeper, muscular planes have to be systematically blocked before incision of the skin is made; (2) by *nerve block*—here the solution is injected in the proximity of the particular nerve, or nerves, supplying a part. For example, the upper extremity can be anæsthetized by bathing the brachial plexus with solution above the clavicle. In the author's view, the best drug for all purposes is novocain, and in particular he favours the French variety, neocain. Maximum safe doses are for 0·5 per cent., 500 c.cm., 1 per cent., 150 c.cm., 2 per cent., 60 c.cm., but the average dosage is less than this. Adrenaline is added to the solution in all regional work.

The Margin of Safety and Technique of Spinal Anæsthesia

In reviewing the available literature on spinal anæsthesia, Shuler F. Fagan and W. D. Wightman (*Current Researches in Anæsthesia and Analgesia*, January–February, 1933, xii, 34) state that a brief summary reveals 75 deaths in a series of 250,000 cases. This résumé showed also that only 40 of these deaths were really attributable to the anæsthetic. In the authors' own review of the spinal anæsthesias given at the Los Angeles General Hospital, where they have a clinic, they find that approximately 15,000 spinal anæsthetics have been given with an average of about one death to every 2,000 cases which could be directly secondary to the anæsthetic. In their private practice they have a series of approximately 1,500 cases with no deaths. It has been their experience that it does not incite acidosis. They do not use spinal anæsthesia where blood pressure is below 100 millimetres of mercury, nor do they use it in the extremely nervous patient, or in the extremely young patient. In order not to complicate the cause of death they usually use local instead of spinal anæsthesia in moribund cases that are operated upon. The advantages of spinal anæsthesia are complete relaxation, quiet respirations, contracted intestines, a lack of direct irritation to the kidneys, liver and lungs, and the absence of direct effect upon the metabolism of a patient with diabetes mellitus. It has come to stay and is a safe anæsthetic when used in properly selected cases. The authors do not subscribe to the opinion that spinal anæsthesia may be administered by anyone who can do lumbar punctures. It is safe in experienced hands and, instead of doing away with an anæsthetist, spinal anæsthesia requires one of greater training due to greater frequency of serious complications.

Post-Operative Pulmonary Complications

From statistics based upon two years' personal observation of the post-operative pulmonary complications occurring in the General Surgical Services of the Massachusetts General Hospital, Donald S. King (*Surgery, Gynecology and Obstetrics*, January, 1933, lvi, 43), finds that purulent bronchitis develops in quite a large percentage of patients after operation. In 47 per cent. of these cases there has been sufficient bronchial obstruction to give rise to atelectasis, but 11 of the 13 fatal cases were true bronchial pneumonias, without evidence of preceding atelectasis. In practically any given type of operation, the percentage of complications is at least twice as high for men as for women, and the author comes to the conclusion that complications occur especially in males following operations on the stomach and duodenum, gall-bladder, and intestines. Pre-operative sepsis and perforation, as well as malignancy and poor general condition, are important factors. Seasonal and pre-operative respiratory infection play a minor part. From the statistical standpoint, the type of anæsthesia is apparently without significance.

End-Results in the Injection Treatment of Varicose Veins

Reports of the end-results in the treatment of varicose veins by the injection method are, on the whole, so favourable that less experienced workers in this field might assume that this type of treatment is next to infallible. Henry H. Faxon (*New England Journal of Medicine*, February 16, 1933, ccviii, 357), believes that the publication of the figures from his clinic, based on the study of 314 cases examined in some instances as long as three years after the last injection, may be of constructive value in correcting this impression, and may be of assistance in preventing reduplication of errors which he may have made and is confident are being made in other clinics. The solution employed in this series was that advocated by Génévrier and endorsed by Douthwaite of 13 per cent. quinine hydrochloride and 6 per cent. urethane; 20, 30 and 40 per cent. sodium salicylate solutions were used in forty-two injections, 20 per cent. sodium chloride in twenty-eight, and 50 per cent. glucose in nine, but these represent too small a number to be of any real significance. By the injection method alone of treating varicose veins, 63 per cent. of 314 cases followed for an average period of 1·4 years showed recurrences. Twenty-five per cent. of the total number showed new varicosities. In the same series over a similar period of time, 28 per cent. were relieved of pain, 19 per cent. relieved of œdema, and 61 per cent. of the ulcers were healed. In a large number of the cases the patients' attitude toward the results was more favourable than the author believes was warranted. Only the 314 cases that returned for follow-up observation of over 613 cases treated up to the time this study was undertaken are used as a basis for this report. Faxon concludes that primary high ligation of the main saphenous trunk when this is varicosed is a necessary adjunct to the injection method of treatment, if the best results are to be secured. The practice of stripping the vein, in part at least, of its blood before injecting, and restricting the injection solution to the area treated for an appreciable time after injecting, will give better results when the large varicosities are being dealt with. Continued support of ulcer cases over an indefinite period after the lesion has healed is often desirable. Quinine hydrochloride with urethane is the preparation of choice, although exceptions to its exclusive use may arise.

Favourite Prescriptions

In Espine Ward's little book, *Favourite Prescriptions*, the third revised edition of which has just been published (London : J. and A. Churchill, 1933. Pp. viii and 148. Price 7*s.* 6*d.*), there are a large number of useful prescriptions, among which we note :—

For chilblains.

℞	Tinct. capsic.		
	Tinct. cannab. ind.		
	Ol. cajuput.	*aa*	ʒss
	Spt. camph.	*ad*	℥i

Sig. Apply the liniment.

For constipation, in adults :

℞	Ext. casc. sagr. liq.		♏ xv
	Ext. glycyrrh. liq.		♏ x
	Tinct. nuc. vom.		♏ viiss
	Tinct. bellad.		♏ v
	Glycer.		ʒi
	Aq. menth. pip.	*ad*	℥ss

Sig. Take three times daily after meals and gradually reduce.

For acute eczema :

℞	Zinc. oxid.		
	Amyli	*aa*	ʒi
	Menthol.		gr. i
	Paraff. moll. alb.	*ad*	℥i

Sig. Apply as directed.

For food poisoning :

℞	Pot. iod.		gr. v
	Chloral. hydr.		gr. v
	Phenol		gr. i
	Liq. hydrarg. perchlor.		♏ xx
	Spt. ammon. aromat.		♏ xx
	Aq. chlorof.	*ad*	℥i

Sig. Take every four hours.

REVIEWS OF BOOKS

Report of the Medical Research Council for the year 1931–1932. London: H.M. Stationery Office, 1933. Pp. 140. Price 2s.

THE Medical Research Council which, set up before the War, has since then been so skilfully and successfully directed by its secretary, Sir Walter Fletcher, has just issued its eighteenth annual report. As before, this shows the extremely wide distribution of its encouragement and help to those undertaking original investigations likely to advance the science of clinical medicine. The Council co-operates with other Governmental Departments, such as the Ministry of Health, the Scottish Department of Health and the three Defence Services. Though the grant in aid of £139,000 provided by Parliament was £9,000 less than in the previous year, the Council has been helped to finance important lines of research by several benefactions; for example, a grant from the Trustees of the late Lord Leverhulme enabled a scheme of investigation into the preventive problems of malaria to be put on a satisfactory basis for five years in London by a team of workers under Sir R. Christophers, lately Director of the Malaria Survey of the Indian Medical Service; the Rockefeller Foundation of New York has generously endowed in perpetuity the Directorship of the Research Department at University College Hopital, which has been held with such distinction by Sir Thomas Lewis, working under the Medical Research Council since 1916; the Research Department now in formation at the National Hospital, Queen Square, has been assisted by the Halley Stewart Trustees. The promotion of clinical research, in which the human subject is the immediate object of scientific study, has always been prominent in the policy of the Council and is specially commented on in this report. There is much interesting information summarized in the account of the activities of the National Institute for Medical Research at Mount Vernon, Hampstead, under the Director, Sir Henry Dale, and of workers at other centres. Among the various researches at the Institute, one on the sex hormones, under the direction of Dr. A. S. Parkes, has recently been organized. During the year Sir Frederick Andrewes, whose services to the Council are gracefully acknowledged, has died; he leaves a report upon the results of more than seven years' work on the classification of the hæmolytic streptococci.

Diseases of the Skin. By the late ROBERT W. MACKENNA, M.A., M.D. Third edition, revised and enlarged by ROBERT M. B. MACKENNA, M.A., M.D., M.R.C.P. London: Baillière, Tindall and Cox, 1933. Pp. 506. Illustrations 194, of which 45 are coloured plates. Price 25s.

ROBERT MACKENNA died in September 1930, and thereby the British School of Dermatology lost one of its most scholarly and far-seeing representatives, and his colleagues a very kindly and courteous friend. As is well known, he was a novelist of ability, and his scientific communications were always heard with interest and pleasure on account of their keen philosophy and original style. The first edition of his textbook appeared in 1923, and was at once accepted as one of the most lucid and practical guides for students and practitioners; a revised and enlarged edition, with coloured plates, followed in 1927, and the present reviewer still possesses a letter from its author testifying almost pathetically to the labour that the revision involved. The task of preparing the present volume has naturally been undertaken by his son, who has incorporated a judicious selection of the more recent advances in dermatology and added nine coloured plates, the choice and reproduction of which are excellent. It retains, of course, the individuality of the former editions, so that it is far easier and pleasanter to read than the majority of " textbooks for students and general practitioners "; the clinical descriptions on the whole are exceptionally clear, the problems of etiology fairly discussed, and the directions for treatment of the common and important diseases are detailed and, as a rule, sound.

There are, however, certain sections which are open to friendly criticism. The most important of these, perhaps, is that on prurigo, in which the prurigos of Hebra and of Besnier, and, judging from one of the photographs, prurigo nodularis, are hopelessly confused. It is curious that, in spite of the clear differentiation between these forms of prurigo that has been made in this country, and by Civatte's masterly analysis in France, this confusion should still exist even among expert dermatologists both here and abroad. Hebra's prurigo and prurigo nodularis, being rare, are of comparative unimportance, but Besnier's prurigo is extremely common, at least in its milder localized form affecting the ante-cubital and popliteal spaces, and its associations make it one of the most interesting dermatoses to general physicians. The reviewer, however, has yet to meet with a purely dermatological textbook in which it is dealt with clearly and adequately. The chapter on eczema is also confusing, though not more so than in most textbooks. The statement is made that " its etiology is obscure." It is true that we have no knowledge of an intermediate substance, responsible for the particular reaction of the skin that we label " eczema " and comparable to histamine (or the H-substance of Lewis) upon the liberation of which the urticarial wheal depends, but, apart from this, the causation of eczema is at least as clear as that of, say, bronchitis, and our conception of it is based on far more scientific data. Surely in a modern treatise it is an anachronism to state that " there *are* three schools of opinion as to its causation " (the italics are ours), as if eczema were a specific disease, and thus to imply that we have got no further than to take our choice between the doctrines of Hebra, Unna, and the old French school. Moreover, little attempt is made to differentiate between the clinical varieties of eczema according to their etiology, and the section of treatment is largely based on the topography of the eruption. There is no clear description of infective eczematoid dermatitis, or of the differential diagnosis and treatment of the forms of eczema occurring in infants. At the end of the chapter is a paragraph concerning circumscribed [illegible] lichen simplex of Vidal, *névro-*

dermite), whereas pruritus in general, pruritus senilis, and pruritus ani and vulvæ are considered separately as neurodermatoses. Circumscribed prurigo is very frequently of psychological origin, and often occurs at the anus and vulva; it is a neurodermatosis par excellence, whereas pruritus senilis and many forms of pruritus ani and vulvæ are not necessarily so. In the description of urticaria, angeio-neurotic œdema and dermographism some reference to the classical work of Lewis and his collaborators ought surely to have been included, and the exact relationship between the first two conditions should have been explained. In a work as up to date in many respects as this a fuller and more accurate account of the sarcoid group of eruptions is called for, based on Schaumann's conception of benign lymphogranuloma. No mention is made of the deposits in bone, with their characteristic radiographic appearances, or of involvement of the lymphoid tissue and viscera, and the statements that in cases of the multiple benign sarcoid of Boeck there is " frequently tuberculosis of the lungs and glands," and that lupus pernio is " often found in association with true lupus vulgaris " are erroneous. Granuloma annulare is considered as " belonging to the lichen group," a view to which few will subscribe, although its causation is as yet unknown.

These criticisms are made in the hope that certain essential revisions will be made in the next edition. The book possesses so many excellent and original features, and is fundamentally so sound, that it deserves the care and labour necessary to remedy its present shortcomings.

Diseases of the Eye. Practitioner's Series. By ANDREW RUGG-GUNN, M.B., F.R.C.S. London: Wm. Heinemann (Medical Books), Ltd., 1933. Pp. 182. Illustrations 21 (8 in colour). Price 12s. 6d.

THE author presents the subject of ophthalmology to the general practitioner less as an isolated speciality requiring difficult diagnostic methods and more as an important part of general medicine wherein the ocular manifestations are the heralds of pathological changes elsewhere in the body, such as increased intra-cranial pressure, cardio-vascular and renal disease, diabetes, syphilis, tuberculosis. Even in the chapter on errors of refraction the medical aspects are those chiefly considered, mathematical and optical details being omitted. The morbid histology, pathology, etiology, symptoms, signs, treatment and prognosis of diseases of the conjunctiva, cornea, sclera, iris and ciliary body, lens, vitreous, choroid, retina, optic nerve, eyelids, lacrymal apparatus and orbit are described. The accounts of the circulation of intra-ocular fluids and glaucoma are well done. The classification of clinical types is up to date and good throughout the book. A chapter is devoted to the extrinsic muscles of the eye and the appendix contains the materia medica of ophthalmology. The author gives detailed accounts of the management of those eye diseases that can be treated by the general practitioner and has drawn attention to those conditions that require the supervision of an ophthalmic surgeon or the resources of a fully equipped institution. Prescriptions of lotions, drops, ointments and other simple therapeutic agents are recorded. All matter outside the scope of general practice, such as surgical technique and descriptions of elaborate diagnostic instruments is omitted or only mentioned briefly. The sections of the work are well arranged, and the author's lucid style makes the reading of this book easy as well as profitable for students and general practitioners. The figures and illustrations are clear.

Workmen's Compensation : its Medical Aspect. By SIR JOHN COLLIE, C.M.G., M.D., D.L., J.P. London : Edward Arnold and Co., 1933. Pp. vii and 160. Price 7s. 6d.

THE first of the Acts bearing on Workmen's compensation was passed in 1897, thirty-six years ago, and as Sir John Collie has had more than thirty years' experience of their working, he writes with an authority probably unrivalled and certainly with the greatest clearness about their practice. Originally the Home Office anticipated that 150,000 accidents would annually come within its scope, but in 1930 the number of accidents for which compensation under the present Act was paid amounted to 461,130; and the author considers that the door of compensation is now almost as wide open as even the extremists could desire. Ordinary patients consult a medical practitioner in order to get well, but the litigant sent for medical examination by his solicitor, by special arrangement with the defendant, must be approached from a rather different aspect, and the point of view of the simulator must be taken into consideration. In drawing up the medical report it should be remembered that neither lawyers nor insurance companies are impressed by medical terms, that it should be written in plain language, and based on facts and not on intuitions. There is much sound advice on the legal aspects and especially in the chapter dealing with the law of libel, and the giving of evidence. The text is illustrated by a large number of cases decided in court.

Syphilis des Herzens und der Gefässe. By Prof. Dr. ED. STADLER. Dresden and Leipzig : Theodor Steinkopff, 1932. Pp. xi and 82. 8 figures and 4 plates. Price 6·50 marks.

THIS little work (which constitutes the 16th volume of "Medizinische Praxis") is a careful, methodical, extremely concise handbook on cardiac and vascular syphilis. Each of the main sections is followed by a recapitulation (printed in italics) of the more important points. The author concludes that cure is possible in tertiary syphilitic affections of the cardio-vascular system and may even occur spontaneously. He believes that specific anti-syphilitic treatment should be employed, but with great care and discrimination, as the cicatrization connected with the process of cure may occasionally lead to coronary stenosis and angina pectoris and grave myocardial symptoms. Ordinary heart treatment must of course be seen to, as required by the symptoms. Stimulating effervescent baths are not advisable, when the syphilitic process is active, as they throw increased work on the heart. The book can be thoroughly recommended to all those who read German. It may be noted that in the bibliography the only English work mentioned is the textbook of Sir James Mackenzie (2nd German edition, 1923). On p. 8 it is pointed out that Warthin's findings as to the frequency and quantity of spirochaetes to be detected locally in syphilitic myocarditis have not been generally confirmed. In the historic portion (p. 13) the date 1728 is given for Lancisi's work and 1827 is given for Morgagni's work, but Lancisi lived 1654–1720, and Morgagni 1682–1771.

Brompton Hospital Reports. Vol. I, 1932. Published by the Research Department of the Hospital. Pp. 144. Figs. 27. Price 2s. 6d.

THIS neatly got-up volume contains fifteen recently published papers by members of the staff of this famous hospital, and presumably is the successor of the reports previously brought out by the Research Department of the Hospital, to which reference is made in Dr. Wingfield's interesting article on the problem of the child in the tuberculous household. Among the other six articles on tuberculosis there are three on tuberculosis in children, an investigation financed by the Halley Stewart Fund, two on sanocrysin and one, reprinted from THE PRACTITIONER, on laryngeal tuberculosis by Sir J. Dundas-Grant, who also writes on the nasal element in asthma. There are three articles on intra-thoracic malignant disease; on bronchial carcinoma (Dr. Atkin): a valuable summary of our knowledge of thymic tumours, with an account of a case, by Drs. Bosanquet and Lloyd, and an authoritative statement on the surgical treatment by Mr. Tudor Edwards. The subject of chronic non-tuberculous infection of the lungs in children is considered by Dr. F. H. Young, intra-laryngeal injection of lipiodal by Dr. W. J. Fenton, and empyema by Mr. Tudor Edwards.

The Infant: a handbook of Management. By W. J. PEARSON, D.S.O., M.C., D.M., F.R.C.P. and A. G. WATKINS, M.D., M.R.C.P. London: H. K. Lewis and Co., 1932. Pp. 47. Price 2s. 6d.

THIS is a useful little book, in which the more simple and practical points in connection with the care and feeding of infants are briefly and clearly set out. It is a handy volume, not only for medical students, but for general practitioners, who will find many of its hints and prescriptions valuable.

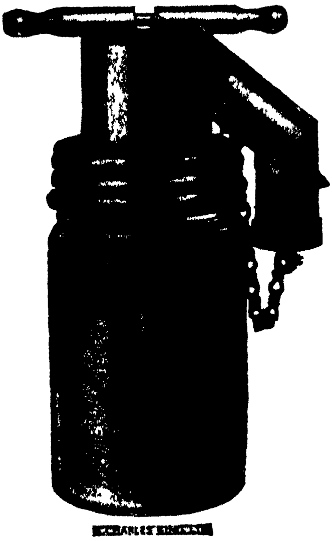
Gray's Anatomy. 25th edition, edited by T. B. JOHNSTON, M.B., Ch.B. London: Longmans, Green & Co., 1932. Pp. 1478. Figs. 1303. Price 42s.

WE reviewed the 24th edition of this famous book at some length in December, 1930 (cxxv, 763), and in this new edition we note that there are 131 new illustrations, the section on surface anatomy has been re-written, and the text throughout revised. Dr. T. B. Johnston, of Guy's Hospital, is a worthy successor to a line of eminent editors.

NOTES AND PREPARATIONS

MODIFIED JUNKER BOTTLE FOR MATERNITY ANALGESIA

Dr. Z. Mennell (Senior Anæsthetist and Lecturer on Anæsthetics, St. Thomas's Hospital) writes: Under existing circumstances in this country, there is no question that chloroform is the only satisfactory anæsthetic for general use in maternity work. It is not strictly true to speak of what is required as an anæsthesia, for it is really an analgesia which is only sufficient to give a partial amnesia. The modified Junker bottle shown in the illustration is an attempt to produce a machine which is fool-proof and which cannot be made to produce a chloroform vapour sufficiently concentrated to cause anæsthesia. The essentials in this bottle are:—(1) It cannot be over-filled. (2) It cannot be fitted up improperly. (3) It will not produce anæsthesia. (4) It cannot be upset in any position. The afferent and efferent tubes do not reach the surface of the chloroform, so that it is immaterial to which of them the bellows is fitted. The key to this little machine is the by-pass between the two tubes which are fitted into the head of the bottle, and on the bore of this depends the maximum strength of chloroform vapour which can be used.



This bottle has been registered and the President of the College of Obstetricians and Gynæcologists, Dr. Fairbairn, has consented to accept the registered design. This has been done to prevent so-called improvements being placed on the market. Messrs. A. Charles King, Ltd., of Devonshire Street, have taken great interest in the construction of this bottle, which has been designed in such a way as to keep down the price.

FILIVEX LIVER EXTRACT

Filivex powder and liquid are potent and palatable preparations of fish liver for the treatment of pernicious anæmia made by the Glaxo Laboratories (56, Osnaburgh Street, London, N.W.1) in accordance with the technique described recently by Professor L. S. P. Davidson, of Aberdeen University (*British Medical Journal*, August 20, 1932, ii, 347). Clinical tests have fully confirmed the conclusions come to by Professor Davidson in that paper, that fish liver extracts have an extraordinary hæmopoietic potency, quickly restoring the blood-picture in pernicious anæmia to normal, and acting at least as promptly as preparations of mammalian liver. The cost of these fish liver extracts is very much lower than that of preparations of mammalian liver, the saving to the patient on each dose of extract equivalent to eight ounces of fresh liver being at least fivepence.

SPIRONINE

Spironine is a palatable elixir, of which each drachm contains 3 grains of di-iodo-caffeine hydriodide together with the soluble constituents of 7½ grains of coffee. It is, in effect, a combination of iodine with caffeine, and is intended for the treatment of asthma and chronic bronchitis. Iodine is well-known to be beneficial in bronchial affections generally, while caffeine has a specific action on muscle tissue and is also a stimulant of the respiratory centre. It is not claimed that spironine is a cure for asthma, but it is recommended for the relief of the intermittent respiratory paroxysms which distress the patient so much. It is given at the onset of an attack, and its effect is usually immediate. In addition, spironine is of value in general practice as a cardiac stimulant.

HARROGATE TABLE WATER

We have received samples of Harrogate Spa sparkling table water, which is bottled and aerated for the Corporation of Harrogate from one of Harrogate's many springs, called spring No. 88, by Messrs. Camwal, Ltd., who are the sole concessionaires. The water is entirely natural, and no special medicinal virtues are claimed for it. From a personal trial we can affirm that this water "mixes" excellently with both non-alcoholic and alcoholic fluids, and certainly compares more than favourably with those of its foreign competitors which are known to us.

COW AND GATE MIXING MEASURE

We have received a new "Cow and Gate" mixing measure, which is made in white enamel, with blue edging, and is graduated in pints, ounces and tablespoons. It is specially shaped to enable it to be used for warming feeding bottles as well as for mixing purposes, and seems to us to be unusually well made and excellently adapted for these purposes.

BRITISH HEALTH RESORTS

A conference on British health resorts took place in Bath on March 4th, with the Right Hon. Douglas Hacking, M.P., the only lay member of the General Medical Council, in the chair. On the evening of March 3rd a reception was given at the Pump Room by the Mayor of Bath, and there was also an exhibition of British and foreign travel propaganda. At the conference on the next day, the work of the recently formed British Health Resorts Association was described by Lord Meston, the president, and discussed from the medical standpoint by Lieut.-Col. R. H. Elliot and Dr. Charles Buckley. Sir Humphry Rolleston spoke on the service of spas to the public, and was followed by Dr. Fortescue Fox, Lieut.-Col. W. Byam, and Dr. F. J. Poynton who emphasized the necessity of linking up spas to scientific medicine.

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THE EVOLUTION OF ENDOCRINE TREATMENT

By SIR HUMPHRY ROLLESTON, Bart., G.C.V.O., K.C.B.

Physician Extraordinary to H.M. The King.

THE branches of therapeutics, of which treatment by extracts of organs, and especially the ductless glands, is one of the most active and interesting, have had an empirical stage and a progressive scientific development. Organotherapy or opotherapy, to employ modern terms, is a very ancient practice; thus among primitive races the heart of a slain enemy was eaten in order to absorb his courage, and in the tenth century some well-known medical authorities treated diseases of the viscera by the administration of the organ thought to be affected, for example, lung substance for pulmonary affections and the lung of the long-winded fox for patients short of breath. On the other hand, it is little more than forty years ago that this " substitution " treatment was justified by the guidance of the experimental method, especially the work of Moritz Schiff and Victor Horsley, as will always be exemplified by a great practical advance—the administration of thyroid for myxœdema by G. R. Murray in 1891. The knowledge of the internal secretions at the beginning of this century became complicated by the realization of the endocrine balance; this led to the conception of pluriglandular deficiency, and imagination outstripping the solid basis of fact, brought forth an endocrine polypharmacy which still persists.

Like medicine, endocrinology as a science and art depends largely on the fundamental help of physiology, as is shown by the epoch-making advances in recent times. In the last century the control of the body was satisfactorily explained by the nervous system; now the chemical messengers or hormones of the endocrine organs share in the regulation of the visceral mechanism to a degree which is becoming progressively more obvious and convincing. The two parts of the autonomic system—the sympathetic and the parasympathetic—are closely associated in their action with two bodies of known chemical constitution, adrenaline and acetylcholine, respectively, which appear to be liberated and to be concerned in the production of the active responses following stimulation of these nerves (Elliott; Dale). As is shown by the recent work of Professor Harvey Cushing, of Boston, and the writings of Professor John Fulton, of Yale, the central representation of both the sympathetic and the parasympathetic is in the hypothalamus, in the close neighbourhood of the pituitary gland which in its turn probably exerts a controlling influence over the other endocrine glands; further, there is, on the one hand, a well-marked nervous connection between the hypothalamus and the posterior lobe of the pituitary or neuro-hypophysis, and on the other hand, the secretion of the neurohypophysis has, by means of a recently described "portal system" of its vascular supply, access to the controlling nuclei of the autonomic system in the adjacent hypothalamus, and evidence is accumulating to show that these centres are stimulated by this secretion.

The conception of neuro-humoralism as the controlling mechanism of the internal environment of the body—the *milieu intérieur* of Claude Bernard (1878), who originated the term "internal secretions" in 1855, and the "homeostasis" of W. B. Cannon (1930), has very wide bearings. In this connection the pituitary presents problems which are complex and perplexing, as, indeed, is obvious from its influence on the processes connected with growth, the functions of the sexual organs and reproduction, some of which are considered elsewhere in this number (vide pp. 525, 534). So many reactions, some of them antagonistic, for example, diuretic and anti-diuretic, have been described as due to extracts of individual endocrine glands, especially the posterior lobe of the pituitary, that the question has arisen whether each different reaction indicates the existence of a corresponding active principle, or whether the site and particularly the condition of the tissues acted upon, play the determining part in the character of their response.

In addition to insulin, other active extracts have been obtained from the pancreas; like other tissues, it has been found to yield a substance with a depressing effect on the arterial blood pressure; recently Santenoise, of Nancy, has isolated, and separated from insulin, a hormone which he calls vagotonine, as it stimulates the vagus and parasympathetic; it also exerts a depressor effect on arterial blood-pressure, which differs from the immediate onset produced by histamine, choline, adenosine, peptone, and other hypotensive extracts of the pancreas, such as kallicrein, which have been previously described; the fall of pressure due to vagotonine is delayed for half an hour or so, gradually increases, lasts a long time, and is never followed by a hypertensive reaction, such as may follow other tissue extracts. It also exerts a hypoglycæmic action; pure insulin, on the other hand, does not lower the blood pressure, specimens which have done so, it would now appear, being contaminated with vagotonine. This new hormone has, on account of its action on blood pressure, been employed clinically on eighty patients with hypertension of various kinds by Abrami, Santenoise, and Bernal; it did not influence all the patients, but in thirty, out of the eighty, a lasting fall of blood pressure followed a series of hypodermic injections; the beneficial effects were specially obtained in the subjects of paroxysmal hypertension, and it was considered to diminish the secretion of adrenaline and impair its activity. It was successful in cases which had been but slightly influenced by bleeding, lumbar puncture, injection of acetyl-choline, and inhalation of amyl nitrite. Conversely, cases irresponsive to vagotonine reacted to hypodermic injections of methyl-acetylcholine. The usual dose of vagotonine, 20 to 40 milligr., does not have any serious ill-effects, and does not alter the blood pressure of normal persons.

An interesting comparison might be drawn between the hormones of the endocrine glands and the accessory food factors or vitamins which have been called "extraneous hormones" (Abel). In both instances diseases are due to their absence or deficiency; myxœdema and cretinism, Fröhlich's adiposo-genital dystrophy and Simmonds' disease (pituitary cachexia), Addison's disease, parathyroid tetany, and diabetes mellitus are analogous to the deficiency diseases scurvy, rickets, beri-beri and pellagra. That excess of vitamins, such as irradiated ergosterol, may cause disease has been shown experimentally in rats, and there is thus in "hypervitaminosis D" a counterpart to hyperthyroidism and exophthalmic goitre, acromegaly, hyperinsulinism or hypoglycæmia, and hyperparathyroidism.

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ENDOCRINOLOGY OF THE MALE GONADS

By KENNETH WALKER, O.B.E., M.A., M.B., F.R.C.S.
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OBSERVATIONS based on castration experiments may be regarded as the earliest contributions to the study of endocrinology. The castration of bulls has been practised ever since agriculture has been sufficiently developed to make use of animal labour, and it may be that the castration of man for special purposes dates from a still earlier period. Nevertheless, although the observation of castration effects is incredibly ancient, it is only within comparatively recent times that the real study of the internal secretion of the testis began. The actual year in which the doctrine of the internal secretion of the testis was born was 1889, when Brown-Séquard described before a meeting of the Société de Biologie the results of his experiments on himself with subcutaneous injections of fresh orchitic extract. The fact that Brown-Séquard's conclusions must now be taken with a certain amount of doubt does not affect the statement that his lecture probably did more than anything else to draw attention to the whole conception of internal secretion, a conception which was due to Claude Bernard in 1855 and hinted at by de Bordeu in 1776 and by A. Berthold in 1849. Brown-Séquard's suggestions indicated to physiologists a fruitful field for investigation, and gave to medicine the hope of an entirely new therapeutic weapon. Although the centre of interest afterwards shifted to the thyroid because of the greater possibilities offered by that gland to the new science of organotherapy, the fact that it was Brown-Séquard's researches that led to the subsequent triumph of thyroid therapy lends to the subject of the internal secretion of the testis a special interest.

A complete study of the male hormone would entail a historical survey of inconvenient length. Brown-Séquard's observations, while they may have given an impetus to subsequent developments, were as inaccurate as they were incomplete, and a great deal of work has had to be done in order to arrive at our present state of advancement.

It is important to remember that the severity of the effects of removal of the gonads differs in various animals and at different periods of life. Among fowls for example, castration of the male results in the comb remaining small, the spurs comparatively undeveloped and the male instincts suppressed. The plumage is, however, but slightly affected by the operation, so that the capon outwardly resembles a cock rather than a hen. These changes may be summarized by saying that in the case of a cockerel the result of castration is infantilism. Removal of an ovary from a hen on the other hand causes the hen to assume to a very large extent the characteristics of the cock. The comb grows in size and what is more remarkable still, the plumage takes on to a great extent the characteristics of that of the cock; in other words, the result of castration in the case of the hen is not infantilism, but masculinization. In mammals it may be said that as a general rule the removal of the testis has more effect on development than does removal of the ovaries. The changes brought about by castration of the male are well known, namely, the development of subcutaneous fat on the hips and thighs, growth of the breasts, a female distribution of the pubic hair, wide-spread changes in the growth of the bones, and a failure to develop the male deep voice and facial hair. Diseases or congenital deficiencies in the ovaries, however, are not so much productive in the human being of male characteristics as of infantilism. Masculinization in girls, when it occurs, is not usually the result of diseases of the ovaries, but of the suprarenals.

These differences in the responses of the tissues to endocrine influences in the case of the two sexes all serve to emphasize the fact that the action of the sex hormone is not so simple as was at first sight believed. Another factor suggesting this is the existence of an interesting condition known to biologists as bilateral gynandromorphism. The best example of this was the bullfinch described by Poll. In this bird the male and the female plumages were sharply separated on the two sides of the body, the right side of the breast being red as in the case of the normal male and the left side grey as in the female. On the right side was found a testis and on the left an ovary. All these observations serve to emphasize that the development of secondary sex characteristics cannot any longer be regarded as resulting simply from the direct action on the tissues of the hormones elaborated in the gonads.

It would, however, be impossible in an article of this nature to go further into this interesting matter, and for our purpose it is sufficient to remember that the part played by the sex hormone is a less simple one than was at one time believed. Not only is the precise action of the male hormone still in doubt, but so also is its origin. Although the majority of sexologists have accepted Ancel and Bouin's theory that the interstitial tissue of the testis secretes the male hormone, many observations have been brought forward in support of the idea that the elaboration of the hormone is not confined to this tissue. Among these observations may be mentioned the fact that there is not any relation between the number of interstitial cells present in the testis and the degree of masculinization of the animal. Indeed, in many of the lower animals such as the triton no cells resembling the interstitial cells of Leydig can be found, while in the mole and in birds which have a definite cycle of sexual activity, the interstitial cells are less apparent during the breeding season than during the period of quiescence.

But interesting as these speculations are, it is with the clinical aspect of the subject that we are chiefly concerned. Medicine has for a long time known that there are certain clinical conditions in the production of which a deficiency of the male hormone plays an important part, for example, cases of eunochoidism and Fröhlich's syndrome. There is also the condition of old age which is associated with a decline in sexual activity and which rightly or wrongly has been linked up in medical speculations with the idea of a deficiency of sex hormone. For a great many years attempts have been made to deal with these conditions by administering male hormone. The means by which this has been attempted have been the following: the giving of extracts by the mouth or by injection, and the carrying out of such operations as grafting and vaso-ligature. It must be confessed from the very start that these methods have all met with very little success. Although I have been experimenting with the oral administration of testicular extracts for a great many years, I cannot recall a single case in which positive results have been obtained. When it is remembered that most of the proprietary preparations on the market are made from desiccated and defatted rams or bulls' testicles and that in the defatting process most of the hormone is lost, it is not surprising that the so-called extracts are inert. Moreover, since it is probable that the digestive juices destroy what hormone remains, oral administration may be regarded as useless. But even when we eliminate the destructive action of digestion by employing injections, the results are very discouraging. At one time I kept under careful observation a large number of patients injected with a fresh extract of bull's testicle prepared for me at the Lister Institute, but I was unable to observe any changes that could be put down to the injections. The explanation of the contrast between the effects of administering testicular and thyroid extract is obvious. Whereas in the thyroid the presence of a large amount of colloid material permits of the storing of great quantities of hormone, very little storage capacity exists in the testicle. That this is the case has been conclusively proved since the male hormone has been isolated in a state of purity. Recent research has identified the male hormone with an oxyketone having the formula $C_{16} H_{26} O_2$. This product, when injected into a capon, has the effect of stimulating the growth of the comb and wattles and of restoring the atrophied spurs. Its action is so apparent that it is now possible to measure the quantity of hormone present in any extract in terms of cock units, one cock unit being defined as that amount of extract which will increase the size of the comb 20 per cent. above the initial value in the course of ten days.

Experiments by many observers have proved (i) that the amount of hormone present, say, in a pound of bull's testicle is very small, and (ii) that in order to restore the comb and wattles of a capon to their normal size, at least ten times the quantity will be required when administered by mouth, than when injected subcutaneously or intramuscularly. It has also been shown that the physiological actions observed are confined to the secondary sex characters, and that injections of male hormone in the doses in which they have, up till now, been given have little or no effect on metabolism, behaviour or bodily vigour. Whether the absence of response in these directions is due to the fact that they are influenced by other hormones than that which has been isolated, or whether it is due to an insufficient dosage has not yet been settled. It is, at any rate, clear that with the products so far available there can be little hope of restoring vigour to the aged or neurasthenic by means of injections. Moreover, even when we confine our attention to secondary sex characters it would probably be necessary in the case of a man weighing 150 lbs. to inject daily at least the equivalent of 15 lbs. of bull's testicle in order to obtain the action produced on the capon. These deductions made by Koch on the basis of his animal experiments indicate the inefficacy of our present methods of male hormone therapy.

Fortunately for future prospects another means of obtaining male hormone has now been discovered. It has been shown that "proviron" (the name now applied to the isolated male hormone) is excreted in the urine. What is especially interesting is the discovery that this hormone is found not only in the urine of men, but also of women. The following description of the method of obtaining it from this source is taken from the writings of Casimir Funk and Benjamin Harrow. The urine is first strongly acidified and then extracted with chloroform for eight hours. The chloroform is afterwards drained off and distilled, and the residue from the distillation treated under reflux with sodium hydroxide. The product obtained by these means is repeatedly extracted with ether, and finally the ethereal extract evaporated, and the residue taken up in oil. One c.cm. of the final product will be found to contain 10 cock units, each cock-unit representing the equivalent of about 125 c.cm. of urine.

This discovery that the male hormone can be obtained from urine is undoubtedly of great importance to clinical medicine. If we were dependent for our supplies only on extracts from bulls' testicles it is unlikely that male hormone therapy would ever become a practical method of treatment. When discussing the subject with the writer two years ago Professor E. C. Koch stated that even with the resources of the Chicago slaughter-houses at his command he could only obtain sufficient hormone for laboratory purposes, and he gave it as his opinion that unless other sources of supply could be obtained, a sufficient quantity of extract would never be available for medical purposes. Fortunately there is every reason to believe that with an improvement in the method of abstraction from urine a sufficient quantity of hormone will some day be forthcoming, and that we will have at our disposal the means of curing cases of testicular deficiency.

The failure of male hormone therapy in the past has acted as a stimulus to efforts in other directions, such as testicular grafting and attempts to increase the amount of male hormone in the body by means of vaso-ligature. That these methods might prove successful in the human being was suggested by the encouraging results obtained in the laboratory. Steinach and many other workers had shown that the secondary sex characters of castrated animals could be restored by the implantation of grafts. Voronoff has since claimed that equally good results can be obtained in human beings; but it must be confessed that very little reliance can be placed on his observations. Other workers have failed to obtain any striking results from the simpler method of vaso-ligature. However much we may be impressed by what has been done in the laboratories we must admit that neither vaso-ligature nor the implantation of grafts has met with equal success in clinical medicine. Temporary benefit may sometimes have been obtained, but within a comparatively short space of time the engrafted tissues are absorbed and the patient relapses into his previous state. This absorption of grafts takes place even when the tissue engrafted is human in origin. It is still more rapid when the material has been supplied by a lower animal.

There is available to medicine, however, yet another means of increasing the amount of male hormone in the body. It has long been known that there exists a reciprocal action between the gonads and the anterior pituitary; not only is the activity of the testis stimulated by extracts of pituitary, but the pituitary is affected by the activity of the gonads. If an animal is castrated, what have been termed "castration cells" appear in the anterior pituitary. These cells are probably basophile cells which are normally present, but which become modified and increased in number after gonadectomy. But it is with the action of the pituitary on the gonads rather than with that of the gonads on the pituitary that we are chiefly concerned. Engle and other observers have shown that an extract of anterior pituitary causes an increase in the size of the testis, the increase affecting both the seminiferous tubules and the interstitial tissues. These and other experiments have therefore opened out another field for medical enterprise. If we cannot make good a deficiency in male hormone directly by the use of testicular extracts or by grafts, we can attempt to do so indirectly through the pituitary. Until proviron becomes a commercial possibility it is this indirect method that probably holds out the best chances of success. Realizing this fact, I have for the last three years been employing an extract of anterior pituitary prepared in Professor Crew's experimental farm near Edinburgh, and although it is always difficult to assess results, it would appear that the use of this extract has been beneficial in certain cases of testicular deficiency. I have also given the same extract to patients suffering from aspermatogenesis for which no apparent cause could be found, on the ground that Balawenetz has reported that injections of anterior pituitary hastens the formation of spermatozoa and spermatids in immature animals. Other observers have, however, failed to establish a connection between the pituitary and gametogenesis and this together with the absence of positive results in my own patients, throws doubt on the validity of Balawenetz's conclusions.

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RECENT ADVANCES IN FEMALE SEXUAL PHYSIOLOGY

WITH SUGGESTIONS REGARDING THEIR POSSIBLE THERAPEUTIC VALUE

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As a result of the researches during the last few years on female sexual physiology the whole conception of this intricate subject has almost completely changed, and indeed is still altering. It has long been known that the ovary has an internal secretion and it had been surmised that the corpus luteum produced a special one, but it is only during the last three years that these hormones have been isolated. For many years it has been known that the ovaries have supreme influence over menstruation and that after oophorectomy menstruation ceases, but it is only lately that we are beginning to realize the intricate nature of menstruation and the number of different hormones concerned in its production. The ovary secretes two distinct hormones with totally different and often antagonistic actions, one from the Graafian follicle known as œstrin and the other from the corpus luteum called progestin.

The chief function of *œstrin* is to cause enlargement and increased vascularity of the uterus, but the administration of œstrin alone never causes menstruation, which entirely depends on progestin. Œstrin is produced in the Graafian follicle, the corpus luteum, and the placenta, and it is also found in the amniotic fluid and in foods, such as potatoes, sugar beet, yeast, rice, and wheat. It is also present in large quantities in the urine of pregnant women. Œstrin and testicular hormones are apparently identical in nature. Experimentally œstrin inhibits conception, and in rodents produces abortion, probably by exciting uterine contractions; this might suggest the possibility of inducing labour or abortion by œstrin; but as the necessary dose for human beings would be so large, this has not been tried.

Progestin inhibits ovulation and sensitizes the endometrium to receive the fertilized ovum; it also causes the pre-menstrual changes in the endometrium. If the ovum is fertilized, progestin supervises the nourishment of the ovum, as is demonstrated by the fact that removal of the corpus luteum during the first three months of pregnancy is followed by abortion. At a later date removal does not cause abortion as the chorion has taken on some of the nourishing functions and a placenta has definitely formed. Progestin also inhibits uterine contractions and, if it could be produced in sufficient amount, would therefore be almost a specific in preventing abortion.

The secretion of the posterior lobe of the pituitary has now been known for a considerable number of years, and its action on the pregnant uterus and unstriated muscle in general has been thoroughly investigated, though it was only recently that it was discovered that there were two, instead of one, active principles present, an oxytocic factor, which acts on the uterine muscle principally and a vaso-pressor which has its main effect on the vessels. Until quite recent times it was supposed that the anterior pituitary lobe was connected with growth only and that pathological conditions of it accounted for dwarfism and hypophyseal cachexia (Simmonds' disease) on one hand, and giantism and acromegaly on the other. In the last few years or so, however, it has been shown that the anterior lobe has other important properties, in fact the whole system of ovarian secretion and menstruation is apparently under the control of the anterior pituitary.

It was first discovered that when the anterior lobe was removed the ovaries atrophied and then there was a complete suppression of œstrin, whereas grafts of the anterior pituitary re-established these functions. It was then found that injection of anterior pituitary extract into immature female mice produced the ordinary ovarian cycle, namely, maturation of the follicles, ovulation, secretion of œstrin, hæmorrhage into the enlarged follicles, and the formation of corpora lutea. Thus it was discovered that the anterior lobe produces a hormone which evokes both œstrin and progestin. It is thought by some—Wiesner[1] in particular—that two definite hormones are present, rho I and rho II, or prolan A and B, the former evoking œstrin and the latter causing luteinization with the formation of progestin. If that were the case the administration of rho II would be most valuable in preventing abortion, and many satisfactory results have been obtained by using Wiesner's extract of this substance; it is, however, possible that the œstrogenic hormone may be present also and perhaps in large quantities when, instead of preventing abortion, it would conduce to it; therefore at present, at any rate, when the presence of two hormones is doubtful and the absolute separation impossible, the administration of rho factors in cases of abortion may be a double-edged sword. Wiesner and Zondek, however, state that the urine of pregnant women contains the rho II factor only, as rho I, being very unstable, rapidly becomes inert on standing and therefore the hormone extracted from such urine should be most effective in causing luteinization, if this was defective or absent, and it is this preparation that has given good results in many cases[2]; unfortunately, the results in my experience are not always good. The urine of pregnant women has proved to be a fruitful source of rho factors, the amount being large, even in early pregnancy, and increasing up to the fifth month, when it gradually diminishes. The œstrin in the urine, however, is greatest at the end of pregnancy. These two observations may be of use with regard to treatment (*vide* p. 540). The injection of rho factors in large doses into an immature female mouse produces rapid luteinization; and this has been taken into account by Aschheim and Zondek in elaborating their test for the diagnosis of pregnancy, which gives a correct result in over 98 per cent. of cases, even in very early pregnancy.[3]

Technique.—Six injections of 0·4 c.cm. of urine are injected into immature female mice twice daily for three days. On the fifth day after the first injection the ovaries are removed, when it is usually possible to see with the naked eye, if the urine is from a pregnant woman, a definite red spot in the ovary representing an exaggerated corpus luteum. If one of the mice shows this, or in doubtful cases if luteinization is found microscopically, the woman is presumably pregnant. Associated with the luteinization there is also well-marked enlargement of the uterus.

This reaction is also positive in hydatidiform mole and chorion-epithelioma, and, indeed, is so delicate that it has been suggested that these two conditions might be diagnosed by a positive reaction when the urine is diluted twelve times, which would give a negative result in an ordinary pregnancy. The test is also very valuable in the diagnosis of chorion-epithelioma after evacuation of a hydatidiform mole; it thus indicates its presence long before clinical features justify a certain diagnosis, and operative removal much earlier and renders the ultimate prognosis much better; this was well shown in a case in my ward last summer.[4]

Early pregnancy can now be diagnosed with certainty in five days instead of delay of at least a month as in the past; it has, indeed, been thought that five days is too long to wait for a result, and a test has been elaborated by Friedman which, however, appears not to be quite so accurate. A rabbit that has been isolated for thirty days to prevent any chance of mating is injected intravenously into the vein of the ear with 4 c.cm. of urine thrice daily for two days, after which it is killed and fresh corpora lutea or hæmorrhagic spots show a positive result. Another test has been evolved by Brouha: immature male mice are injected with small quantities of pregnant urine for 8–10 days; enlargement of the seminal vesicles is a positive reaction.

While excision of the anterior-pituitary lobe suppresses ovarian function, castration is followed by increased size and functional activity of the anterior-pituitary; this suggests that one of the ovarian hormones has an inhibitory effect on that lobe and, as there is a high pre-menstrual content of œstrin in the blood, that œstrin probably inhibits the anterior-pituitary, which causes regression of the corpus luteum, and so menstruation. According to this hypothesis the cycle is as follows: the anterior-pituitary hormone evokes the formation of œstrin from Graafian follicles which rupture and luteinization occurs, again due to the anterior-pituitary; but the corpus luteum produces besides progestin an excess of œstrin which passes into the blood and inhibits the anterior-pituitary, thus causing regression in the corpus luteum with sudden cessation of œstrin production, thus starting menstruation. It has been shown clinically that bleeding occurs two days after removal of corpus luteum, no matter at what period in the cycle. The whole cycle is therefore under the control of the anterior-pituitary which, however, has not any direct action on the uterus, the essential cycle being carried out through the ovarian hormones.

How may these recent advances bear on the physiology of pregnancy, labour and lactation? In the first place the implanted ovum is dependent on the corpus luteum, as is shown by abortion when the corpus luteum is removed during the first three months of pregnancy. The corpus luteum, however, is dependent on a hormone produced by the growing ovum; later the placenta produces a luteinizing hormone analogous with the anterior pituitary hormone and after that time the corpus luteum grows no bigger and shortly after begins to regress. Its removal after the formation of the placenta does not cause abortion. There are numerous hypotheses about the causation of labour, though none as yet is entirely satisfactory or proven; but it was only a question of time before the newer facts about female physiology would be put together to formulate a new hypothesis of its causation, and this has been done as follows: The placenta contains progestin at six months, but not at full term; and it has been shown by Robson[5] that "pitocin," the oxytocic principle of the posterior-pituitary, does not cause any definite uterine contraction in the earlier months of pregnancy after which its action increases until it reaches its maximum at full term. It is also known that injection of progestin can prolong pregnancy and that as progestin decreases there is a large increase in the production of œstrin towards the end of pregnancy. Taking all these factors into account it may be surmised that œstrin sensitizes the uterine muscle to the action of pitocin, but that before the sixth month the secretion of progestin inhibits any sensitivity of the muscle to pitocin; further, as the weeks advance, the progestin gradually decreases and finally disappears, whereas œstrin becomes more and more increased in amount till a climax is reached at the end of the ninth month, when the amount of pitocin circulating in the blood is sufficient to cause the uterine muscle, which has been sensitized by a sufficiently large production of œstrin, to contract and start labour. Progestin may thus inhibit sensitivity of the uterine muscle to pitocin, or it may be that its well-known antagonistic action to œstrin prevents the action of pitocin; but as progestin diminishes œstrin increases and gradually comes into its own, causing an increasing sensitization of the uterine muscle to pitocin. According to this hypothesis it should be possible to induce labour by giving large doses of œstrin followed by injections of pitocin; this has been done in animals by several observers, but the method has not been very satisfactory clinically in inducing labour, possibly because the dose of œstrin required, except at full term, is a very large one for the human being, and sufficient has not been given, whereas at full term, when the woman is producing almost sufficient œstrin, the injection of a little additional pituitary alone very often starts labour.

With regard to lactation, it is known that œstrin produces well-marked mammary hyperplasia, but inhibits milk secretion, which is probably due to a separate hormone produced by the anterior-pituitary, the mamma requiring preparation by œstrin before the pituitary hormone can produce its effect. It is possible, also, that the mamma produces a hormone which causes amenorrhœa while lactation is occurring. This, however, may act directly or through the anterior-pituitary, causing perhaps a persistence of a corpus luteum from post-partum ovulation.

How can all this recent information be utilized in the treatment of obstetrical and gynæcological conditions? In the first place administration of the hormones do not reactivate the general stimulating cells in the anterior-pituitary, but cause increased function in other glands. In a similar fashion the administration of thyroid extract in menstrual disorders is more than substitution. Theoretically four hormones could be used therapeutically, but up to the present time the use of two only is practicable—œstrin and prolan or rho factor. Progestin would be most valuable in nullifying abnormal œstrin influence on the endometrium and thus prevent some cases of functional bleeding and also in the prevention of abortion, but up to the present the source of supply is very meagre, and that source, namely, the corpora lutea of animals, contains an excess of œstrin as well as progestin, and therefore the results would be variable even if a sufficient quantity could be obtained. These difficulties may be overcome by biochemical separation in the none too distant future, when a most valuable therapeutic agent would be obtained. The separation of prolan A and B or rho I and II is doubtful, at present, but according to Wiesner, as rho I is so unstable the preparations of anterior-pituitary hormone consist almost entirely of rho II or prolan B—the luteinizing hormone.

Œstrin, on the other hand, can be prepared with ease from the urine of pregnant women, the placenta and numerous other sources, with the result that there are numerous preparations on the market even now, and the price is by no means exorbitant. Œstrin only acts by causing some hyperplasia in the uterus, and is therefore used chiefly in cases of amenorrhœa, either in young women who have never menstruated or more commonly in cases of what is known as secondary amenorrhœa—the periods having long intervals between or being very scanty. It is best administered orally, for though greater dosage can be given hypodermically, it is quickly voided in the urine, and therefore a large quantity is lost as a therapeutic agent. For the last eighteen months I have been using an œstrin preparation known as progynon in 16 of such cases, and the results would seem to be satisfactory: 11 of the 16 are now cured and need no further treatment; 2 are improved, and only 3 are definitely in no way affected by the treatment. Recently two of these, however, have since menstruated after the injection of large doses of progynon, 1,000–10,000 M.U., but I do not know yet if the cycle will be reactivated.

The anterior-pituitary sex hormone can be given in two sets of cases: in amenorrhœa small doses cause a maturation of the Graafian follicle and stimulate ovarian growth, and would therefore seem to be of more use in primary amenorrhœa with some underdevelopment of the genitalia than œstrin, which acts on a hypoplastic endometrium only. At the present time the chief value advanced for this hormone is in functional uterine bleedings, that is severe bleeding from the uterus not due to any inflammatory cause or tumour, but probably due to some ovarian dysfunction. Rho II acts on the ovaries alone and causes rapid luteinization of a persistent Graafian follicle, thus liberating progestin which, in its turn, may transform pre-menstrual into pre-gravid endometrium and thus bring about cessation of bleeding, or, in other cases, it may activate defective corpora lutea (e.g. corpus luteum cysts) which had caused severe bleeding. If the bleeding is due to the latter cause, defective corpora lutea, the effect of injection of rho factors or prolan should be immediate, but if due to the former, a persistent Graafian follicle, frequent administration for an indefinite period will be required before the granulosa cells are converted into lutein tissue. Similar results are obtained in menorrhagia of puberty, for which prolan is reputed to be almost a specific. Its action is therefore to produce progestin which antagonizes the action of œstrin, which had previously been unantagonized and caused severe bleeding associated with a proliferative endometrium, the ovaries in such cases showing that no corpora lutea had been formed and therefore œstrin had full control of the uterine endometrium. Rho or prolan is destroyed in the gastro-intestinal tract, and therefore must only be given by injection; large doses daily must be given in functional bleeding in which luteinization is necessary. The product is very unstable and therefore those on the market should only be used when fresh.

The injection of the urine of pregnant women has been found to be especially efficacious when prolan is required to be administered, as the supply is plentiful and cheap and the hormone is always active. The hormone is destroyed by boiling, so the urine is best sterilized by passing it through a Berkefeld filter into sterile test tubes; 20 c.cm. of urine, preferably from a woman 2–3 months pregnant, is injected on alternate days for functional bleeding, the urine at this time having an excess of prolan and being fairly free from œstrin; whereas for amenorrhœa, in which some œstrin is a valuable adjunct, the urine should be taken from a woman five months pregnant, in which the proportion is 5 of prolan to 1½ of œstrin, and 3–5 c.cm. can be injected every other day.

Rho factors may also be of use in the prevention of abortion, as already stated, and of late an investigation has been carried out with regard to their action on painful menstruation, it being thought that they would stimulate the action of the uterine musculature and that the contractions would be more rhythmical and less spasmodic. Some excellent results have been obtained, but in my experience it certainly is not a specific for all such cases and failures occur as well as successes. The investigation is, however, still proceeding, and it is possible that the refractory cases may yet yield to a larger dosage. Œstrin also has been given in such cases to correct uterine hypoplasia, a common concomitant of this condition and venous stasis. It is said to allay irritability and good results have also been obtained with this treatment, especially when combined with thyroid extract, which definitely stimulates uterine growth. It is possible that prolan or rho factors may have a beneficial effect on sterility by causing better luteinization and therefore better maturation for and nourishment of a fertilized ovum. Small doses of thyroid in addition may also be of benefit.

In conclusion, there is still a very considerable amount of work to be done regarding sexual physiology and its application to the pathology of ovarian and uterine dysfunctions. When this has been fully investigated there is no doubt that we will have some very valuable therapeutic products in our hands, which will obviate operative treatment in a large number of cases of gynæcological conditions which now can only be cured by operation. During the last 25 years gynæcology has tended to become more surgical than medical, but the pendulum is now swinging back and medicine is reasserting itself once more in gynæcology and will continue to do so for a number of years, after which a perspective will be reached when the true value of medicine and surgery in various conditions will be viewed dispassionately, and an orthodox treatment laid down. At present the whole subject of female physiology is in a state of flux, and there are many enthusiasts who are apt to chase shadows, especially with regard to the therapeutic value of the numerous physiological discoveries which have recently been made, and it is only when these shadows have been thoroughly investigated and either found to be empty or their substance proved that it will be possible to assess the true value of these discoveries and their various applications in the treatment of gynæcological disorders.

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NON-SPECIFIC PROTEIN THERAPY

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NON-specific protein therapy, aptly described as "the ordeal by chill and fire," was the inevitable reversion from an age in which specific vaccine therapy had been overdone and not fulfilled its expectations. Over twenty years ago, when specific vaccine therapy was at its height, a surgeon suggested to Joseph Miller that greater therapeutic benefit might be obtained in bacterial infections if mixed vaccines were used instead of specific, and to prove his point took pus from septic surgical patients and transferred it to a beer bottle containing beef tea, which he incubated. All these cultures were mixed, sterilized by heat and filtered, and the sterilized filtrate was put up in small bottles for therapeutic use. The records showed the subsidence of febrile illnesses after one or two injections, and Miller was impressed with an actual demonstration in cases of acute arthritis in which all signs of pain and swelling had gone in twenty-four hours following a single injection. This was Miller's introduction to non-specific therapy of which to-day he is one of the greatest exponents, and the origin of the vaccine later marketed under the name "Phylacogen." No wonder such results shook the orthodoxy of "specific" therapy.

The value of non-specific therapy had been empirically established many years before, but because it was not in accord with the prevailing mode of strictest specificity was passed unnoticed. Rumpf (1893) treated typhoid patients with advantage by pyocyaneus vaccine; Bokenham (1895) reported that diphtheria antitoxin was effective in typhoidal and streptococcal conditions; Matthes (1895) showed that the focal effects of tuberculin injections could be obtained with proteose; Renaud (1911) found that a typhoid vaccine killed by quartz light radiation had a definite therapeutic effect on a number of inflammatory conditions of non-typhoidal origin. Ichikawa (1912), the first to use the intravenous route, observed that typhoid fever could be modified or terminated by the intravenous injection of paratyphoid vaccine; Kraus and Mazza (1914) reported similar results using *B. coli* vaccine in puerperal infections as well as typhoid; Lüdke (1915) showed that identical results could be obtained with an albumose intravenously; and both Schmidt and Saxl (1916) by the injection of milk intramuscularly.

The agents elaborated in the past fifteen years with the idea of flushing specific antibodies into the circulation are legion, and it is doubtful if any possess the special virtues which their manufacturers claim. They all have one point in common, the ability to cause a more or less febrile reaction, hence the term "pyrogenic therapy." In their clinical application, familiarity with one or two agents and the practical accumulation of personal knowledge of the dose necessary to produce the desired reaction will prove more beneficial in a series of cases than meddling with many. The secret of their use lies in never using them when proven specific measures are available, and when employing them to commence early in the disease, give them slowly, and use small doses at the start. Good prompt reactions can be obtained with typhoid vaccine intravenously, and moderate delayed reactions by the use of peptone or milk intramuscularly. At their best they are only of proven value in a limited number of picked cases of certain diseases, so too much must not be expected of them. Nevertheless, they may keep a patient interested whilst

Nature cures him.

THE CHARACTER OF THE REACTION

No food is allowed for two to four hours before the injection. Within half an hour the patient, if up, is placed in bed and remains there during the reaction. He is allowed copious fluids, and a small dose of codeine or adrenaline may be given to shorten the reaction or lessen the discomfort.

The *chill or rigor* may occur within fifteen minutes following an intravenous injection, usually within thirty minutes, but it may be delayed several hours. Following an intramuscular injection such as milk, it does not usually occur for two to three hours. It generally wears off within half to three-quarters of an hour. Sometimes within six to twenty-four hours there is a second chill. The rigor may consist of actual chilling requiring hot-water bottles, or just muscular twitching and trembling without sensory disturbances.

The *rise in temperature* varies with the patient and the agent employed. With vaccines intravenously the maximum temperature, about 104° F., is reached within three to four hours, and there is a rapid defervescence. With milk intramuscularly the maximum is attained in six to eight hours, and the temperature is normal again in twenty-four hours. Any discomfort is greatly relieved by sponging.

The *increase in pulse rate* varies from fifteen to thirty beats per minute, but the onset of profuse sweating brings it down again to the pre-injection level.

The *blood pressure* shows a slight increase during the chill, but with the sweating there is a progressive decline for six to eight hours with a return to normal in twenty-four.

The *leucocyte count* is extremely interesting. During the rigor there is a primary leucopenia, probably due to the acoumulation of the leucocytes in the internal organs, though others suggest that it is due to a functional paralysis or depression of the bone marrow. This is followed by a leucocytosis which reaches its maximum in four to nine hours, in which polymorphs predominate. There may be a small increase in the monocytes and eosinophils, but the lymphocyte count remains unchanged. This leucocytosis is due in all probability to a release of the leucocytes from the splanchnic to the peripheral blood stream, combined with some bone-marrow stimulation. The erythrocyte and platelet counts increase and nucleated red cells may appear.

The *focal reaction* is the one that interests the therapeutist. Should any inflammatory lesion have existed before the injection, a focal reaction occurs around it within twenty-four hours. The inflammation at first becomes more acute, with an increase of pain, tenderness and hyperæmia. This is succeeded by a diminished reaction, or even by a restitution to normal, leading to a state of euphoria; but in some cases the exacerbation of the inflammation continues and operation on an appendix or gall-bladder may be necessary.

The *serum enzymes* show definite changes following the injection, the proteolytic enzymes and lipases being increased whilst the diastase remains unaltered. No consistent increase in specific antibodies has ever been shown. In other words, though clinically there may be a transient increase in protection against infection or the incubation time of infections be prolonged, the reaction is not necessarily an antitoxic one.

Following vaccines, headache is quite common. Herpes is quite a frequent occurrence, and nausea, vomiting or delirium occasional happenings. The coagulation time of the blood is diminished, due to an increase of fibrinogen and thrombokinase, and the sedimentation rate shortened. The changes in the surface tension of the serum tend to increase osmosis and the penetration of substances into the cells. Metabolism and glandular activity are augmented.

Other interesting changes illustrative of the biphasic reaction following the injection of foreign protein may be set out as follows :—

	Negative phase.	Positive phase,
Blood :		
Reaction	Acidosis.	Long-continued alkalosis.
Ca/K ratio	Reduction.	Increase.
Nitrogen	Increased elimination.	Retention.
Fibrinogen	Diminished	Greatly increased.
Enzymes	Decrease.	Progressive increase.
Complement	Decrease.	Increase.
Capillary :		
Flow	Stasis.	Rapid flow.
Permeability	Increased.	Decreased.
Kidneys :	Anuria.	Diuresis.
Reticulo-endothelial system :	Active phagocytosis.	Lessened activity.
Nervous tone :		
Splanchnic	Parasympathetic.	Sympathetic.
Peripheral	Sympathetic.	Parasympathetic.

Innumerable attempts have been made to shorten or eliminate the negative phase by varying the protein agents or their mode of administration, but it is now believed that without the lytic phenomena of the first stage the therapeutically positive second stage in which there is stimulation of the defensive mechanism of the body will not be adequate. As regards the fate of the injected material, it is thought to be removed from the blood stream by the cells of the reticulo-endothelial system and there fixed.

THEORIES REGARDING THE MECHANISM OF THE REACTION

That non-specific therapy should influence the course of specific diseases was at variance with the current conceptions of immunity, but to support its empirical use and clinical results attention was drawn to the fact that intercurrent fevers frequently ameliorated pre-existing disease processes. Gay and Claypole (1914) suggested that the therapeutic effect of non-specific therapy lay in such a collateral effect as the leucocytosis produced, but the clinical result is not always commensurate with the blood changes. Yet leucocytes may liberate bactericidal bodies or elaborate proteolytic enzymes to split toxic products. Paltauf (1915) considered that the beneficial results were due to the thermogenic substances in the proteins used, but the best temperature reaction is not always associated with the best therapeutic effect. Nevertheless, a state of fever has some direct stimulating effect on preformed antibodies. Rohonyi (1916) thought that non-specific therapy produced some neutralizing substance against the invading bacteria. Herrmann (1918) showed that the intravenous injection of foreign protein stimulated the liberation of specific antibodies in animals in which the previously injected antigen was unable to cause such a liberation. Weichardt (1919) attributed the action to a general stimulation of the blood and tissue cells with the increased production of specific substances, whilst Döllken (1919) ascribed the effect to a selective stimulation of certain organs. Larson (1919) suggested the liberation of so-called " sessile " antibodies which may have been formed but not given off into the circulation with sufficient readiness. Other suggestions came from Starkenstein (1919) who concluded that an alteration in the permeability of the blood-vessels, at first increased, but later diminished, checked the inflammatory process, and from Pemberton (1920) who considered the effect due to an increased catabolism of glycogen. Ling (1925) showed that in normal beings the injection of various foreign proteins caused the shedding of proteolytic, peptolytic and lipolytic enzymes into the circulation within twenty-four hours. Mackenzie and Frühbauer (1927) observed that when rabbits which had some time previously been given egg-white and later had lost all evidence of circulating antibodies were later injected with typhoid vaccine the egg antibodies reappeared.

To this re-awakening of an old immunity they applied the term "anamnesic reaction." Wolff-Eisner (1928) produced further substantial evidence that protein-shock therapy stimulates the specific response to invading bacteria, especially if localized. He employed animals with definite foci of infection and animals with general infections without foci, such as tetanus. Non-specific injections caused the foci to become actively inflamed again and increased the defensive mechanism, whereas animals with general infections became very much worse and many died.

Petersen (1928) believes that the true mechanism combines many of these theories, and suggests that, following non-specific protein injections : (i) there is an increased tolerance to intoxication, due to a decreased permeability of the cell membrane, (ii) the toxic material is more rapidly destroyed, due to cellular stimulation and the mobilization of proteolytic enzymes, (iii) the lymphogogue effect floods the lymph spaces with plasma rich in antibodies, due to the increased permeability of the capillaries, and (iv) the increase in the anti-enzymes in the lymph spaces makes the further proliferation of the bacteria difficult.

NON-SPECIFIC PROTEIN AGENTS

The commoner non-specific protein agents that have been employed may be divided for convenience into four main groups : (1) blood and sera, either human or animal, before or after immunizing injections; (2) proteins of animal or vegetable origin, or their split products; (3) bacterial vaccines or extracts; and (4) tissue extracts.

(1) *Blood and sera :* (a) *Normal.*—Blood, after clotting, probably due to some colloidal rearrangement, behaves as a protein foreign to the host, especially if administered at once. Whole blood, either citrated or untreated, may be given subcutaneously or intramuscularly in doses of 10–50 c.cm., and serum in

doses of 1–3 c.cm. may be injected intravenously, subcutaneously or intramuscularly. The injection provokes a slight rise of temperature with a considerable leucocytosis. It is probable that blood transfusions from healthy adults, if sufficiently large, might neutralize a toxic product or stimulate a resistance to it. Also in many cases a toxin or its resultant antibody circulates in the blood, hence repeated injections of the patient's own blood should assist in desensitization without the trouble of finding out the nature of the antigen.

Auto-serotherapy was introduced by Gilbert (1894) for the treatment of pleurisy with effusion. He withdrew 5–10 c.cm. of effusion and injected it under the skin and claimed that the course of the disease was greatly shortened. This method has been extended to other diseases, and cases have been treated with blister serum, cerebrospinal fluid and joint fluid, as well as by pleural transudates and exudates, but the results have never been convincing.

The normal sera of animals have been employed in therapy from time to time. Normal chicken serum has been used in pneumonia. normal beef serum in anthrax, and normal horse serum in diphtheria (Bertin, 1895) and hæmorrhagic diseases (Weil, 1908). In such cases it is necessary to remember the possibility of a sudden allergic reaction, so the patient must be tested with the foreign serum previously. Smith (1916) used normal horse serum in the treatment of gonorrhœal arthritis and thought the beneficial results were due to a kind of allergic shock. Cecil (1917) also tried normal horse serum in various forms of arthritis with varied responses.

(b) *Immune sera.*—Anti-meningococcal, anti-streptococcal and especially anti-diphtheritic sera have been employed as non-specific agents intravenously, intramuscularly, subcutaneously, and even orally in many other infectious diseases without striking result. Deutschmann (1907) used 2–4 c.cm. of the serum of horses immunized with yeast cells in the treatment of acute infectious diseases and diseases of the eye.

(c) *Antitoxic sera.*—Since the advent of anti-toxin therapy (1894) the common practice of injecting foreign serum has been responsible for many fatal accidents due either to a second dose following after an interval of 10–14 days on a primary dose that has acted as a sensitizer, or to a primary dose being injected into a horse-sensitive individual. In other non-allergic subjects large and frequent doses may produce the disagreeable rather than dangerous condition known as serum disease, but these reactions have been largely obviated by the use of concentrated sera and the giving of aspirin. McCallum (1897) reported the use of diphtheria antitoxin in tuberculosis and tubal infections. Lilienthal (1897) gave it in acute surgical infections; Talamon (1901) used it with considerable success in pneumonia; and Paton (1906) in the treatment of tuberculosis, arthritis and cerebro-spinal meningitis. Tetanus antitoxin has been similarly employed, but on account of the danger of sudden allergic reactions and the comparative inefficacy of the injections, antitoxic sera have fallen largely into disuse.

(2) *Protein solutions.*—(a) *Proteins of animal origin :* Egg-albumen in 5–10 per cent. solution in doses of 5–10 c.cm. subcutaneously has been used to produce shock (van den Velden, 1910), and gelatin in 1–2 per cent. solution in normal saline employed subcutaneously or intravenously in hæmorrhagic conditions. Nowadays milk is the chief agent employed. Cows' milk, fresh or pasteurized, is boiled or allowed to simmer for ten minutes and then cooled. Human milk may take the place of cows' milk, and fat-free milk and purified casein (½–1 c.cm. of a 5 per cent. solution) have been prepared for intravenous use. In general, 2–5 c.cm. of cows' milk are given intramuscularly, increasing the dose every 2–4 days till a maximum dose of 10 c.cm.

is reached, or five injections have been given. The reaction occurs within 5–6 hours, and the temperature may persist for 2–3 days and the leucocytosis for 3–5 days. The intensity of the reaction is thought to be due to the bacterial content of the milk or their derivatives, since fresh sterile milk hardly causes a reaction. Since the milk is subjected to such heating the danger of an allergic reaction in a sensitized individual is not a great fear, though one or two non-fatal cases have been reported.

Milk was first employed by both Schmidt and Saxl (1916) intramuscularly in the treatment of typhoid. Müller and Thanner (1916) were the first to use it in cases of iritis in their ophthalmological practice, where probably nowadays it is most extensively employed. On account of its additional styptic effect it used to be advised in many hæmorrhagic diseases. It has also been suggested in asthma (Schiff, 1923), erysipelas and gynæcological conditions (Gellhorn, 1926). Care must be taken not to introduce the milk directly into a blood vessel for fat embolism may result.

(b) *Proteins of plant origin:* Nucleic acid and the nucleins were used (Horbaczewski, 1891) to stimulate antibody formation, but their use has been superseded by sodium nucleinate, which has no protein. It is given in doses of half a gram subcutaneously or intramuscularly as a 5 per cent. solution. More recently a compound of nucleic acid with hexamine (nucleohexyl) has been employed in doses of 10 c.cm. of a 10 per cent. solution intravenously. Gardner-Medwin (1924) reported good results in the treatment of pneumonia with sodium nucleinate, but in Davidson's experience (1926), though it stimulated an increased production of leucocytes, it had no value as a therapeutic agent.

(c) *Protein-split products.*—These include the deutero-albumoses or proteoses, the peptones and histamine.

The deutero-albumoses or proteoses are prepared from fibrin, gelatin, milk or wheat, and are given daily in doses of ½–2 c.cm. of a 2 or 10 per cent. solution, the dosage being regulated so as just to produce a mild reaction. They were first used by Lüdke (1916) in infectious diseases, especially typhoid, though Matthes (1895) had shown previously that effects comparable to those produced by tuberculin could be obtained with them. Miller and Lusk (1916) found 1–2 c.cm. of the 4 per cent. solution used intravenously beneficial in typhoid fever, confirming Lüdke's findings, and they also noted definite improvement in the joint symptoms in cases of uncomplicated persistent arthritis. Snyder and Ramirez (1921) confirmed the beneficial effects in chronic arthritis using a proteose prepared from milk.

Peptone, for the production of shock, is used in 10 per cent. solution, and 8–10 c.cm. are given intravenously. Numerous peptones, such as Armour's, are produced by the digestion of beef, but Witte's peptone is prepared by the digestion of fibrin. Nolf has used peptone by injection since 1908 in treating the hæmorrhagic diathesis and paroxysmal hæmoglobinuria; Gow (1921) in cases of septicæmia; and Crowe (1923) and Veitch (1924) have advised a course of peptone intravenously as an adjuvant and preliminary to vaccine therapy in cases of arthritis. Peptones were used first in allergic conditions by Pagniez and Vallery-Radot (1916) by the mouth, and by Auld (1917) and Nolf (1919) by injection. A 5 per cent. solution is used intravenously or a 7½ per cent. solution intramuscularly, beginning with 5 minims and increasing by 3 minims twice a week until a dose of about 40 minims is reached.

Histamine is formed by the decarboxylation of histidine, a component of every known protein. Since a substance of such a nature is thought to be released at the site of allergic reactions, and since the natural antagonist to histamine in the body is adrenaline, the secretion of which is probably stimulated, I have been employing it in the therapy of allergic conditions.

The initial dose is a tenth of a milligram subcutaneously, gradually increasing by a tenth of a milligram daily or weekly up to a milligram dose. The characteristic of histamine reaction is shown by the intense headache or throbbing, the flushing of the skin and faintness from the drop in blood pressure. As the dosage increases the reactions become comparatively shorter, probably due to the facilitation of the secretion of adrenaline.

(3) *Bacterial products.*—(a) *Vaccines:* Vaccines are employed largely in the production of non-specific reactions. The experience of Miller's surgical friend Schafer (1911), who employed a mixed bacterial vaccine in all manner of infectious disease with occasional success, has already been referred to in the opening paragraph; but when exploited commercially it soon fell into disrepute. Coley's fluid, a fluid culture containing the products of *Streptococcus erysipelatis* and *B. prodigiosus* in glycerin, frequently ameliorated inoperable cancer and sarcoma, especially the spindle-celled variety. *B. coli* vaccine in doses of 20–25 million organisms for the first injection was used by Perkins and White (1923) and Middleton (1923) in arthritis with arrest of the disease in the early stages. Staphylococcal vaccine was used by v. Jauregg (1913) in the treatment of general paralysis of the insane.

Typhoid vaccine, or the mixed typhoid and paratyphoid vaccine, is the product most commonly employed. A good initial dose is 25–35 million organisms, but some advise as much as 100 million. The dose is increased every 2–4 days by 10–15 million for 5 injections. The reaction is very rapid and often severe. It has been used most extensively in cases of arthritis where good results have been obtained by Miller and Lusk (1916), Cecil (1917), Scully (1917), Thomas (1917), Snyder (1918), Cowie and Calhoun (1919), Cowie (1921), Betz (1921), Campbell (1925), and Yeoman (1926), since when its use has increased. Good results are also reported from its use in gonorrhœal complications (Miller and Lusk, 1916). In syphilitic paresis it is used by some in preference to malarial infection as the frequency of the chills can be regulated, and the treatment is not followed by the severe anæmia and high mortality that frequently complicates the malarial infection (Mackenzie, 1927). In multiple sclerosis 16–20 injections at 1–3 day intervals, and after three months another course of 8–10 injections leads to some amelioration of the condition (Grosz, 1922; MacBride and Carmichael, 1924). It has also been employed (Goodman and Gottesman, 1923) to produce vaso-dilatation in peripheral constrictive or occlusive vascular disease.

(b) *Extracts:* That most commonly employed is tuberculin, which for the tuberculous acts like a virulent poison, whilst for the non-tuberculous it is relatively inert. It was used by v. Jauregg (1909) in the treatment of paresis in large doses of a tenth to half a milligram. Van Leeuwen and Varekamp (1921) introduced the tuberculin treatment of asthma, prompted by the frequency of positive tuberculin reactions in asthmatic patients. Later workers have not been so enthusiastic.

(4) *Tissue extracts.*—Probably the crude and barbaric habit of localized abscess formation, the use of the thermocautery, blistering and rubefacients, and the exposure of patients to various light rays, such as heliotherapy in tuberculosis and other chronic infections, and irradiation in asthma and localized inflammatory processes lead to the liberation of disintegrated tissue extracts and so to the absorption of foreign proteins. On the other hand, definite tumour extracts have been used in neoplastic diseases, cartilage extracts in chronic arthritis and gout, and vascular extracts in arteriosclerosis, to mention but a few with very little benefit. Marrow and splenic extracts have been employed in diseases of the hæmatopoietic system, and various polyglandular extracts in the treatment of

obscure and metabolic disorders. Splenic extract, dealbuminized, in the treatment of tuberculosis and allergic skin conditions is probably one of the latest (Paul, 1929). In tuberculosis 5 c.cm. of the 20 per cent. solution are given hypodermically and repeated twelve times over 18 days. In allergic conditions a 40 per cent. albumen-free splenic solution is given in doses of 5 c.cm. on alternate days for twelve injections. Good results are also claimed from the oral administration of splenic extract. In tuberculosis healing is said to be quickened and allergic skin conditions to disappear within a few minutes to a few days.

Leucocytic extracts were shown by Hiss and Zinsser (1908) to contain antibacterial substances. Consequently horse or rabbit leucocytes were obtained, washed and suspended in distilled water and used in the treatment of infections. They led to a good leucocytosis but caused very little general reaction.

INDICATIONS FOR NON-SPECIFIC THERAPY

In infectious diseases non-specific protein therapy may be applicable, especially in the following conditions: (*a*) in localized rather than generalized infections; (*b*) when foci of infection cannot be reached for culture, or when the organism is unknown or not certainly determined; (*c*) when the organism is known, but where specific therapy is acknowledged or has proved to be of little value; and (*d*) when localized changes in structure prevent sufficient circulation, for the lighting up of an infection during the non-specific reaction may reactivate the healing mechanism. At the same time it is necessary to remember that it may convert a latent into an acute inflammation, such as a tuberculous focus, an appendix, or a gall-bladder.

It is in cases of arthritis that non-specific protein therapy is most commonly employed. In acute cases 70 per cent. of patients are practically free from discomfort after two or three injections, but in only half of these is the relief permanent. The results are best in those cases in which the disease is confined to the peri-articular tissues. In chronic cases good results are obtained in but a very limited number of cases, and then in the atrophic or infective type rather than in the hypertrophic or traumatic type. The usual agent employed is typhoid vaccine intravenously, but the colon bacillus, albumose and milk also have their supporters. Some say that the good results should be attributed not to the injection but to the mechanical effect of the intense muscular contractions during the chill which play an important part in breaking down small adhesions.

In gonorrhœa and its complications, such as arthritis, prostatitis, epididymitis and tubal infections, non-specific therapy often proves more beneficial than specific. Miller and Lusk (1916) used typhoid vaccine intravenously, Müller and Weiss (1916) used milk intramuscularly and Smith (1916) used normal horse serum intravenously. Similar results are often found in dysenteric cases, and the beneficial effects that used to follow protein injections in cases of puerperal infection, septicæmia, erysipelas and cellulitis have been largely improved in recent days by the use of the newer specific streptococcal sera.

In allergic conditions non-specific therapy has been used to advantage. The general tendency to employ it indiscriminately in all cases without testing for possible causes first is to be decried. Avoidance or removal of the specific cause and of contributory factors is the ideal method of treatment, but is possible only in a minority of cases. Failing that, specific therapy for desensitization should be attempted. Non-specific desensitization should only be employed when specific causes cannot be determined or their removal or injection has failed. Auld (1917) first advised the use of peptone in bronchial asthma, and though the brands used have varied from time to time between Witte's and Armour's, Witte's No. 30 is probably the best to-day. The route of administration has varied from the oral as tablets to the rectal as enemas, but the intramuscular or the intravenous routes are generally used. The more recent the disease and the more regularly spaced the intervals the better the result. Peptone has also been suggested as a preventive or palliative measure in hay-fever, but in my experience it will never take the place of specific therapy. In some cases of urticaria, angioneurotic œdema and migraine peptone therapy has brought relief.

Van Leeuwen and Varekamp (1921) introduced the tuberculin treatment of asthma, prompted by the frequency of positive tuberculin reactions in asthmatic patients. One commences with $\frac{1}{10}$ c.cm. of a one in a million dilution and increases the dosage daily or on alternate days. Ling (1928), Simpson and Stone (1929) and Maxwell (1930) have obtained good results in a small number of cases with tuberculin therapy, but in my experience the majority relapse very soon. Schiff (1923) suggested the injection of whole milk as a non-specific agent in the treatment of asthma. The milk is sterilized by boiling for an hour, and $\frac{1}{2}$ c.cm. doses are injected three times a week until 3 c.cm. doses are reached.

Auto-hæmotherapy and auto-serotherapy are employed with advantage in urticaria and angioneurotic œdema, especially of the recurring type, and often they form the only treatment that brings any relief. Blood is withdrawn from a vein at the elbow and reinjected subcutaneously or intramuscularly normally, after defibrination, in doses of $\frac{1}{2}$–2 c.cm. every twenty-four hours or less, or as freshly separated serum in doses of 2–4 c.cm. repeated at two to seven day intervals until a dose of 10 c.cm. is reached. Injections of the mother's serum have proved very beneficial in the papular urticaria of children. Though milk and typhoid vaccine have been tried in the eczema of adults without striking results, a majority of observers have noted the beneficial effects of blood injections in adults, but not in infants. Auto-hæmotherapy has also proved beneficial in cases of dermatitis venenata, generalized and localized pruritus and pemphigus.

In other dermatological conditions non-specific protein therapy has often proved of use, especially in severe, chronic, usually non-responsive conditions. Engman and McGarry (1916) and Scully (1917) employed typhoid vaccine to advantage in cases of psoriasis, whilst others have since reported good results with other vaccines, autoserum and horse serum; and Balassa (1930) describes good results in cases of leucoplakia, kraurosis vulvæ and chronic X-ray dermatitis and ulceration. Others find it beneficial in infections with the large-spored ringworm, in chronic inflammatory patches and sluggish ulcers, and in carbuncles and boils. Low (1932) finds that all forms of protein shock treatment, especially if a temperature is induced, will influence the early stages of syphilis beneficially, but not to such an extent as to warrant their adoption generally either alone or in combination with drug treatment. The position is quite otherwise in the later stages of syphilis, especially neuro-syphilis. In most of the dermatological conditions mentioned non-specific protein therapy increases the susceptibility of the lesions to local treatment and so hastens the cure.

In ophthalmic practice non-specific therapy is frequently employed since Müller and Thanner's (1916) original observations on the use of milk injections in cases of iritis and gonorrhœal ophthalmia, in which condition it is said to act like a specific remedy (Howard, 1927), but Allen (1925) prefers to use typhoid vaccine. Beneficial results often follow the use of milk in cases of keratitis, choroiditis, retinitis, conjunctivitis, corneal ulcers, trachoma, and other severe eye infections. On occasions horse serum has been used in cases of iritis and retinal hæmorrhage, typhoid vaccine in leutic conditions and iritis (Boyd, 1919), and peptone in ocular conditions following acute infectious diseases.

Even as far back as Hippocrates and Galen the beneficial effects of a fever on psychoses had been recognized. It is not remarkable that non-specific therapy should benefit cases of puerperal mania (Barkin, 1929). In general paralysis of the insane, tuberculin, staphylococcal and typhoid vaccines were used prior to v. Jauregg's (1917) malarial treatment. In 30–40 per cent. of the cases a cure results whether the reaction has been brought about with typhoid vaccine or malarial therapy. It is thought that the meninges become more permeable after a non-specific reaction, allowing an increased penetration of anti-substances into regions normally deficient. Peptone, milk and brain extracts have been employed extensively in epilepsy without apparent benefit.

In manifestations of the hæmorrhagic diathesis, such as purpura, hæmophilia, melæna neonatorum and hæmorrhage in the course of disease or after operation, milk has been employed largely on account of its additional styptic effect, but its use has been largely superseded by the various hæmoplastic sera prepared from the horse, rabbit or human. It is in cases in which sera prepared from horses have been used that allergic deaths have occurred, so preference should be given to human sera on this account.

Vaccines of staphylococci and *B. prodigiosus* have been advised in neuritis. The occasional decrease in neoplasms following the injection of bacterial or tumour autolysates has been described. More recently non-specific therapy has been employed to produce vasodilation in Raynaud's disease, thrombo-angiitis obliterans and arteriosclerotic gangrene with gratifying results (Goodman and Gottesman, 1923, and Brown, 1926). Allen and Smithwick (1928) treated 25 cases of long-standing peripheral vascular disease with intravenous typhoid vaccine. There was a definite relief of pain and a beneficial change in the appearance of the lesions. The injections were thought to hasten the development of an adequate collateral circulation. Naurison and Millman (1930) also confirmed these results. Schindler (1928) used non-specific protein therapy to inhibit peristalsis in peptic ulcer, and Kolischer (1929) used whole blood injections intramuscularly in cases of nephritis and reported beneficial results.

CONTRA-INDICATIONS TO NON-SPECIFIC PROTEIN THERAPY

Untoward reactions occur in less than 1 in 200 cases treated and in less than 1 in every 500 injections. Any unusual reaction generally occurs after the initial dose, so it is as well to be familiar with the diseases which are contra-indicated and the type of reaction which occurs. Infancy and age have not been considered contra-indications (Hench, 1932).

Non-specific therapy should not be used in the following cases: (*a*) marked arteriosclerosis or uncompensated cardiac, renal or vasomotor disease, for deaths from arterial thrombosis or anuria have occurred. Hæmaturia and nephritis are occasional complications after injections, even in presumably normal people; (*b*) in generalized or chronic multiple infections of long duration, or states of exhaustion following prolonged illness, because it is impossible to stimulate fatigued cells; (*c*) in pulmonary tuberculosis, active or quiescent, because severe focal reactions or acute pleurisy generally occur; (*d*) in conditions in which hæmorrhage may occur, as in hæmophilia, epistaxis, the ulcerating stage of typhoid fever or dysentery, or within a fortnight of operation; (*e*) in chronic alcoholism because patients frequently develop delirium tremens; (*f*) during pregnancy because severe uterine contractions may be stimulated; and (*g*) in allergic conditions the special protein used should be tested to determine whether the patient is hypersensitive to it or not.

BAD SURGICAL RISKS

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NO surgeon who has been in practice for any length of time can have failed to notice that certain types of person react badly to operative interference. A review of these types, and an effort to discover in them some common abnormal characteristics, may provide a scientific explanation of the clinical facts, and so lessen the dangers to which operation must expose them. A bad surgical risk may be defined as a type of patient whose prospect of recovery from the active surgical treatment of his condition falls much below the average. Essentially hazardous procedures, such as the removal of a pulmonary thrombus or the excision of an œsophageal carcinoma, are therefore not under consideration. Cases which may be described as bad surgical risks fall naturally into two main groups, a physiological and a pathological; but the dividing line is so difficult to draw that the introduction of an intermediate group has been found necessary.

CLASSIFICATION

Physiological group : (1) Age. (2) Sex. (3) Build and physique. (4) Race. (5) Social status and occupation.

Intermediate group : (1) Temperament and mental instability. (2) Excessive smoking, alcoholism and drug addiction.

Pathological group : (1) Lesions of nervous system. (2) Toxæmias and general infections. (3) Bronchitis and asthma. (4) Cardio-vascular lesions. (5) Blood conditions; hæmophilia and anæmia. (6) Pancreatic inefficiency and diabetes. (7) Hepatic inefficiency and jaundice. (8) Renal inefficiency and uræmia. (9) Endocrine derangements. (10) Local conditions.

Age.—During the first 36 hours of life, operative interference is borne relatively well; perhaps this is due to the fact that no nourishment, other than that already contained within the body of the child, is necessary for its subsistence. After this first 36 hours follows a period during which surgical interference is badly tolerated. About the eighth or ninth day, however, surgery again becomes safer. For the last four thousand years advantage of this second brief period of better toleration has been taken by the Jewish race. From the ninth day until the end of the third month, operative procedures that can be should be delayed. From the third year until the last epiphysis joins, at the age of 25, operations are better borne than at any other period of life. It may not be out of place here to refer to the fact that children born during the last two years of the war are prone to have a low resistance to infection and trauma. During the middle period of life, when the struggle for existence reaches its maximal intensity, the sudden enforced halt in an active wage-earning life, coincident with operation, is undoubtedly a factor which produces worry and upsets the capacity for rest which is so essential to recovery. After the early fifties, when the degenerative processes of age are beginning to manifest themselves, operations are surprisingly well tolerated. In extreme old age they again become hazardous.

Sex.—During the menstrual period, and at the menopause, women bear operations badly. The increased risk at these times is readily accounted for by the metabolic upsets and disturbances in circulatory and nervous systems which accompany them. Women are also bad subjects for gastrectomy. With these exceptions, they are better risks than men, they do not suffer from shock to the same extent, and their blood-forming capacity seems to be better. They themselves attribute this to a capacity for facing trouble more bravely than the males, who, on the other hand, consider women to be less susceptible to pain.

Build and physique.—Lightly built and wiry persons are better risks than the heavily built and muscular. The very thin, owing to high metabolic rate and lack of nutritional reserve, are poor risks. Operations can, however, be performed upon such with much greater rapidity than in those who are more generously covered. Fat persons are grave risks, particularly for abdominal operations.

Race.—The worst racial risks with which we have to deal are the Jews; the Welsh rank next to them. It is generally thought that the limit of human toleration to trauma is shown by the Chinese, but I am informed by those who have worked among them that this applies only to the lower classes and that the educated and cultured Chinese do not show this characteristic.

Social status and occupation.—Generally speaking, the higher the social status, the worse the operative risk. This is in all probability due to the favourable conditions under which the upper classes have lived for many generations interfering with the processes of natural selection in weeding out the weaker elements of their stock; to in-breeding, and to over-development of the mental as compared with the physical side. This process of survival of the fittest was unchecked in the lower strata of society until the last few decades. They also escaped over-education.

Occupation.—Those who lead hard lives, sailors, farmers, clerks, colliers and navvies, are good risks. Successful business men, publicans and butchers, all of whom tend to be overfed, are poor risks. Musicians and many other possessors of the "artistic temperament" make unfavourable patients. Either the fear of death or mistrust of their fellows makes most clergymen, doctors and nurses bad patients.

INTERMEDIATE GROUP

Temperament and mental instability.—The phlegmatic, unimaginative type, in which the emotions are not strong and in which cortical control is adequate to the small demands made upon it, make good risks. The higher type of individual, in which the emotions are more strongly developed and the cortical control proportionately greater, although in an equally good state of balance, more readily exhibits the phenomena of shock. Those in whom this balance is disturbed display the various stages of mental derangement with which we are familiar. The degree of derangement depends not only upon the degree of loss of control, but also on the normal or pathological state of the subconscious mind. This unbalanced class, ranging from the temperamental individual on the one hand, to the maniac on the other, although all grave trials to their surgeon, are not necessarily all bad risks. The mentally deficient and the manifestly insane are, as a rule, good risks. The temperamentally unstable and the neurasthenics are the cases we have cause to fear. The former, not infrequently, completely lose their balance after an operation. The latter fight against everything that is done for them, and, instead of showing a reasonable degree of faith in their doctors and nurses, endeavour to direct their own treatment. It is interesting to note that abnormal variations in blood sugar have been observed in certain of the psychoses.

Drugs.—Tobacco: Those who do not indulge in tobacco take anæsthetics better than those who do. Cigarette smoking produces irritability of the pharynx and respiratory passages. This gives rise to a tendency to cough, not only during the induction of an anæsthetic, but for several days after its administration. Pipe and cigar smoking have a less deleterious effect from this point of view, but heavy smokers require more anæsthetic than those who smoke little. When time permits, smoking should be stopped for a few days before operation. If acid drops are sucked, instead of a pipe, the condition of the patient will be improved and his craving for tobacco relieved.

Alcohol : Heavy drinkers are resistant to anæsthesia. They also tend to be unduly fat and to suffer from hepatic inefficiency. Sugar relieves their craving and enables the amount of alcohol usually taken to be diminished. It also improves liver function. In this type of individual, the occasional production of delirium tremens by operative interference must be remembered, and some alcohol must be allowed throughout the operative period.

Morphine : The undiagnosed morphine addict is a very grave operative risk. That the patient will have taken care to have a considerable stock available for the emergency is practically certain. Under the influence of operative stress and discomfort, his craving will lead him to take it more liberally and frequently than his needs demand. His reactions to operative interference will puzzle his surgeon and all those who are looking after him. If a confirmed morphine addict is known to be taking from 1½ to 3 grains daily, this amount should be allowed throughout the operative period. No habitué can reduce the amount below a daily allowance of 1½ grains without discomfort; this he will not tolerate. He will be difficult to anæsthetize and his resistance to local anæsthesia must be seen to be believed. He will not suffer from shock and, if his constipation can be overcome and he escapes infection, he will make a recovery that compares very favourably with that of his less self-indulgent brethren. *Cocaine:* Devotees to this drug exhibit tachycardia, excitability, and mendacity, and are notoriously bad risks. Addicts of other hypnotic drugs may be regarded as mentally unstable.

PATHOLOGICAL GROUP

Lesions of the nervous system.—The anæsthetic and trophic changes associated with these conditions are the principal matters we have to consider. They cannot be overcome, but they are a very definite indication for gentleness, the most essential attribute of all good surgery. They also entail the more frequent inspection of a clean wound than is ordinarily advisable, because some of the defensive mechanisms, notably pain, are absent, so that wound complications do not produce the symptoms which would otherwise draw attention to their onset. *Epilepsy:* The occurrence of an epileptic fit during anæsthesia may lead to death. In the post-operative stage it may lead to bursting of stitches or slipping of ligatures. An unsuspected cerebral tumour may cause death from respiratory failure, if lumbar puncture is performed.

Toxæmias.—The importance of eliminating septic foci in the mouth, nasal sinuses and throat has not only been warmly advocated by those who specialize in dentistry and in ear, nose and throat work, but is recognized by all thoughtful physicians and surgeons. It is particularly important to keep this in mind in any operation on the respiratory or alimentary tracts. The presence of staphylococcal skin infections, acne, and seborrhœa greatly increases the risk of wound infection. Of the generalized chronic infections, the one most often met with is due to colitis, and is characterized by the presence in the urine, either constantly or intermittently, of the *Bacillus coli* with its accompanying *Streptococcus fæcalis.* This infection may best be controlled by the administration of large quantities of fluid and by encouraging the growth of the lactic acid bacillus in the cæcum. Acute streptococcal conditions should be treated with large doses of scarlatinal serum. Except in cases of peritonitis associated with obstruction, the administration of *B. Welchii* serum has proved disappointing. *Tubercle :* The liability of this condition to be lit up by operative interference has been recognized for many years. The evacuation of a collection of tuberculous pus, or of the ascitic fluid in tuberculous peritonitis, are noteworthy exceptions to this generalization. A severe operation in the actively tuberculous is equivalent to the administration of an over-dose of tuberculin, and is prone to have the same disconcerting results. Tuberculous patients are also particularly prone to develop keloid and hypertrophic conditions in their scars. *Syphilis :* The nervous, cardio-vascular, hepatic and renal systems are being considered separately. Apart from derangements in these systems, the syphilitic is quite a good risk.

Bronchitis and asthma.—No patient suffering from a common cold should be operated upon except in cases of real emergency. The risk of doing so is far greater than is generally realized, and it must be remembered that an avoidable risk is an unjustifiable one. Not only is the anæsthetic less well taken, but the risks of post-operative chest complications, notably collapse of the lung, are greatly increased. Coughing and sneezing not only tend to burst stitches and produce hæmatomas, but are exceedingly painful. Rest is disturbed, and the post-operative period becomes one of anxiety and discomfort. Those who suffer from bronchitis and asthma should, whenever possible, be operated upon during the summer months. They are better subjects for local than for general anæsthetics. In them abdominal wounds should always be reinforced with interrupted non-absorbable sutures. Their post-operative course is still more disturbed and uncomfortable than that of the patient with the common cold. The ordinary expectorant mixtures are not well tolerated during the first few days after an operation, and a certain degree of refinement in prescribing is called for. Patients suffering from hay-fever should not be operated upon during June and July, when their trouble is usually at its worst.

Cardio-vascular lesions.—Patients with cardiac œdema or other gross signs of heart failure should not be operated upon. Cases with compensated valvular lesions seldom die on the operating table. They are, however, prone to develop embolism during the post-operative period. Cases of myocardial degeneration also stand the actual operation surprisingly well, but are liable to die unexpectedly about the fourth or fifth day afterwards. About ten days later there is a second danger period. I have observed this phenomenon in cases operated upon under spinal or local anæsthesia, as well as in those who have been given a general anæsthetic. The acute toxic heart is the condition that is responsible for deaths during operation. Patients with arteriosclerosis and high blood pressure stand the actual operation well; if they escape post-operative lung complications and severe post-anæsthetic vomiting they usually follow a normal course, but the strain of vomiting or coughing, if severe, is more than the degenerated vessel wall can stand.

Blood conditions.—Hæmophilia : This condition can only be satisfactorily treated by blood transfusion. It yields better to one large transfusion than to repeated small ones. Minor degrees of interference with coagulability may be dealt with either by repeated small transfusions or by the injection into the blood stream of 5 c.cm. of a 10 per cent. solution of calcium chloride, on three successive days. The intravenous administration of 30 c.cm. of a 30 per cent. solution of sodium citrate has also been found useful. *Anæmia:* Unless time permits of slower forms of treatment, no case of anæmia, where the red corpuscle count is as low as three million, should be operated upon without preliminary transfusion. Deficiency in the volume of circulating fluid may be treated by gum infusion. Patients with *leukæmia* should have preliminary X-ray treatment. The vitamin deficiency of *pernicious anæmia* should be treated by liver extract and other forms of vitamin, given in conjunction with hydrochloric acid, which enables them to be absorbed. Preliminary treatment on these lines diminishes the likelihood both of hæmorrhage and of suppuration. In *splenic anæmia* the operative prognosis depends in large measure on the blood platelet count. When this is raised, there is a tendency to thrombosis; when it is lowered, hæmorrhages are liable to occur.

Diabetes.—One of the most striking advances in safety in surgery is seen in the treatment of diabetics who have to undergo operation. Except in severe septic conditions, which neutralize the effects of ordinary doses of insulin, and in cases that have a high degree of arterial degeneration, they can be brought almost to the level of normal risks. It must be remembered that the removal of foci of acute sepsis in diabetics brooks of no delay. The presence of such a focus further lowers the already damaged carbohydrate tolerance, and needs an increase of insulin seemingly out of all proportion to the extent of sepsis. Cases requiring urgent operation should receive 20 units of insulin and 30 or 40 grams of dextrose one hour before operation. From 2 to 4 drachms of sodium bicarbonate should be given at the same time. In operations that are less urgent, about 20 units of insulin, balanced by 20 grams of dextrose, should be given every four hours until the urine sugar is reduced to a mere trace. The insulin may now be cut down to 10 units with 20 grams of dextrose at the same intervals, unless the urine sugar is materially increased when the dose is lowered. Sodium bicarbonate and large quantities of fluid should be given throughout. More heroic doses of insulin, up to 40 or 60 units, may be required in severe toxic conditions, but a careful watch for symptoms of hypoglycæmia must be kept. As regards anæsthesia, chloroform must not be used under any circumstances. It must be remembered that hyperglycæmia reduces the healing powers of the tissues and favours the development of germs. It is, therefore, particularly important to avoid rough handling of the tissues, and to be scrupulously careful with regard to cleanliness during the operation and after-treatment.

Jaundice and hepatic inefficiency.—The risk of hæmorrhage in patients suffering from jaundice is universally recognized. Post-operative acidosis is also a common occurrence. The presence of bile pigments and acids in the blood diminishes its calcium content. The best means of combatting the risk of hæmorrhage is by the intravenous administration of 5 c.cm. of a 10 per cent. solution of calcium chloride for three successive days previous to operation. The intravenous administration of a 25 per cent. solution of dextrose has also been found to improve the coagulation time and to stimulate liver function. Prolonged jaundice diminishes the bactericidal powers of the liver, and actual degeneration of the specialized Kupffer cells has been observed. Surgical shock is always accompanied by a rise in blood sugar. This is probably due more to an upset of the glycogen-storing capacity of the liver than to interference with its glycogen-forming powers. Histamine bodies are broken up in the liver, and any factor lowering hepatic function is therefore likely to delay the destruction of these substances and to prolong the stage of shock. Whether surgical shock is actually caused by the absorption of these bodies, or is merely associated with their absorption, is not yet definitely proved. Their elimination is hastened by the intravenous administration of a 6 per cent. solution of gum acacia. Recent work on the absorption of glucose by the rectum has shown that blood sugar is lowered more by a glucose enema than by one of ordinary saline. The undoubtedly beneficial effects of glucose per rectum in surgical shock may therefore be due to an actual lowering of the hyperglycæmic condition, and not to the nutrient effects of the glucose, as was formerly thought.

Renal inefficiency.—Very little can be done to modify operative risks in gross kidney disease; chronic parenchymatous nephritis is an exceedingly grave risk. Patients with any form of renal dropsy are hazards that the wise surgeon treats by any method other than operation. Chronic interstitial nephritis may be regarded, from the surgical standpoint, as affecting operative risks only by virtue of the associated vascular changes. These have already been considered. The moderate degrees of impairment of function, that are associated with back pressure or some toxæmic condition, are the only ones over which we have much control. From the operative risk standpoint, these may conveniently be gauged by the blood urea content. Patients with a blood urea of 0·30 per cent. or less are good risks; those with 0·50 per cent. are bad risks; those with a blood urea above 0·60 per cent. may confidently be expected to develop post-operative uræmia. The impairment is dealt with by the gradual relief of the back pressure, by the administration of large quantities of fluid, the limitation of protein intake, rest, and the administration of alkalis. Variations in the renal leak point for sugar have already been referred to in considering diabetes. Alterations in the chloride leak point are of great importance. An abnormally high point is likely to be associated with œdema, and an abnormally low one with dehydration.

Endocrine derangements.—Suprarenal : Mention must be made of Addison's disease; hypoglycæmia and acidosis are very common. Metabolically, Addison's disease is the converse of diabetes. *Thymus :* Most deaths under anæsthetics in early life are liable to be attributed to status lymphaticus. *Pituitary :* The polyuria and obesity associated with some derangements are of interest. They respond to treatment by pituitary extract. *Thyroid :* In thyrotoxic cases iodine should be given in small doses for from 12 to 14 days before operation. The basal metabolic rate is lowered by the inhibitory effect of iodine on thyroxin secretion. The importance of pre-operative rest and avoidance of all excitement has been recognized for many years. At least two weeks should be devoted to this end.

Local conditions.—An operation upon any area of the body that has previously been the site of surgical interference is attended by increased difficulty and consequently greater risk. An abdomen that has been the site of previous laparotomies should only be opened for very definite indications. When there are adhesions to the abdominal wall and when the viscera are matted together, no surgeon can be reasonably certain of a satisfactory operative result.

Conclusion.—The temperamental, the toxic, the obese and those in whom there are gross derangements of metabolism are the cases where much care and circumspection must be exercised. Intelligent pre- and post-operative management will bring them much nearer to the level of normal risks. The work that has been done on carbohydrate metabolism has helped us more, in the treatment of these risks, than any other single factor, and when its ramifications have been still further worked out we shall be able to treat these bad operative risks in a simpler and more rational manner.

THE VALUE OF LIGAT'S REFLEX IN ABDOMINAL DIAGNOSIS

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THE reflexes described by Ligat[1] are superficial reflexes elicited by picking up a definite area of the skin of the abdomen with its underlying subcutaneous tissues. Whenever I examine the abdomen I use the reflexes mentioned in Ligat's articles, and when positive they give most useful and reliable information, enabling one to make a certain diagnosis in a great many cases where it would be guesswork otherwise. Hamilton Bailey states[2] that Sherren was unable to confirm Ligat's observations that there is a hyperalgesic spot midway between the ensiform cartilage and the umbilicus in cases of chronic gastric ulcer. He does not mention the test in the diagnosis of duodenal ulcer or gall-bladder disease, but in cases of appendicitis he considers it to be the method of choice. Ligat's reflex is not mentioned at all in French's " Index of Differential Diagnosis." It is doubtful therefore if the test is widely used, and this article is published in the hope that others will try the reflexes.

In explaining the viscero-sensory reflex, Ligat points out :—

> Afferent stimuli from the viscera are constantly being transmitted to the spinal cord, while reflex efferent impulses are as constantly passing to the muscles, interstitial tissues, and skin of the body wall. We depend on these correlated impulses for the discharge of our normal physiological functions, and in health are quite unaware of their existence. But when an organ becomes irritated, more intense impulses than normal ascend to the group of cells in the spinal cord, which is in direct communication with the organ, and this group of cells, being subject to undue stimulation, forms an irritable focus in the cord. The equilibrium of the viscero-sensory arc is thus upset, and a stimulus, which applied to the corresponding cutaneous surface of the body wall would have given rise to a normal sensory

response in health, now evolves an abnormal one.

The hyperalgesic areas may correspond to one, two or even three spinal segments, but by careful discrimination of the point of maximum hyperalgesia the actual organ affected can be determined in most cases. The area covers a long, narrow, vertical band of skin. If one organ is affected, there is one maximum point with a spread in a vertical direction, the hyperalgesia almost always extending further in a downward than in an upward direction. There is no hyperalgesic spread in a lateral direction.

Though the degree of pain is variable, that provided by pinching is usually severe in acute visceral imflammation. In other cases, mostly those of a chronic nature, in many of which the patient has been complaining of vague abdominal pains only, very careful examination is necessary, as only a slight response may be obtained. In many chronic cases this is the only sign which can be demonstrated. In neurotic patients the limitation and spread of the hyperalgesia never correspond to that found in the true viscero-sensory reflex; but care is needed in examining such patient, and the area must be accurately marked out.

To elicit the reflex the following method is to be adopted: The test should immediately follow inspection of the abdomen: the patient should lie on the back, a low pillow for the head, with mouth slightly open and the arms by his sides. In fact, the patient should be, as far as possible, completely relaxed, both mentally and physically. When pinching, pick up the skin and subcutaneous tissue firmly between the finger and thumb, and draw away from the deeper layers of the abdominal wall, avoiding any downward pressure on the abdominal wall. In some cases, it is difficult or impossible to pick up the skin and subcutaneous tissue and draw them away from the deeper layers, and in these cases I pinch only the skin, using the same degree of pressure at the different areas; in pinching a gradual pressure should be exerted so that only a minimal discomfort to the patient is produced. It is important that the pressure should be applied in the plane shown in Fig. 2. The various hyperalgesic spots are then tested, and if present the direction and area of the hyperalgesia is noted. The test should be done first in the left hypochondriac region, as at this point a normal response is always met with. The facial expression must be watched closely; if positive the patient winces or even cries out if the response is severe.

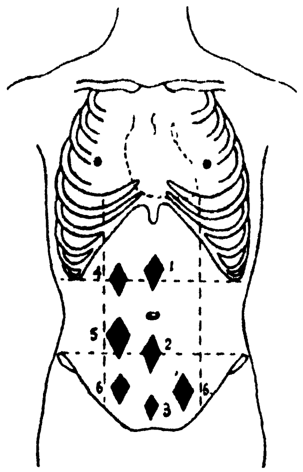

FIG. 1.—1. Gastric and duodenal area. 2. Small-gut area. 3. Large-gut area. 4. Gall-bladder area. 5. Appendix area. 6. Fallopian-tube area.

The diagram shows the areas where hyperalgesia is elicited when present :—(1) *gastric and duodenal area :* maximum point mid-way between ensiform cartilage and umbilicus; (2) *small-gut area :* maximum point at junction of upper and adjacent fourths of a line drawn from umbilicus to symphysis pubis; (3) *large-gut area:* maximum point at junction of lowest and adjacent fourth of a line drawn from the symphysis pubis to the umbilicus; (4) *gall-bladder area :* the maximum point is situated where a horizontal line drawn from the tip of the tenth rib crosses a vertical line drawn midway between the nipple line and the middle line of the abdomen. (As a rule I do not take Ligat's point, but I draw a line from the umbilicus to the nipple and take a point one inch below the rib on this line or in cases where the breast is pendulous, to approximately the centre of the ribs in front) ; (5) *appendix area :* maximum point at junction of inner and middle thirds of a line drawn from the anterior superior spine to the umbilicus; (6) *Fallopian-tube area :* maximum point at junction of lowest and adjacent fourths of a line drawn from the middle of Poupart's ligament to the umbilicus.

Fig. 2 shows the same maximum hyperalgesic points and the arrows indicate the plane and direction in which pressure has to be exerted by the forefinger and thumb when pinching. The results of the tests should be carefully noted in writing at the time, as one finds in some cases these reflexes are a variable quantity, and it is only by comparing the notes of previous examinations that one can interpret them correctly. In some cases repeated observations over a long period have to be made before a definite diagnosis can be arrived at, or in other words, until a positive reflex is elicited. The following case took 11 months :—

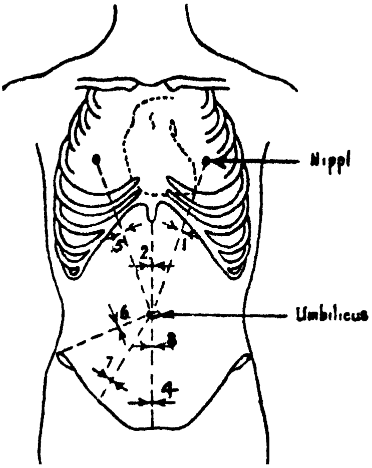

FIG. 2.—1. Initial test area 2 Gastric and duodenal area. 3. Small-gut area. 4. Large-gut area. 5. Gall-bladder area. 6. Appendix area. 7. Fallopian-tube area.

A solicitor, aged 63, gave a history of having contracted syphilis forty years previously. He complained of a tightness in the chest and pains down the backs of the arms on exertion; occasionally after hurrying he was sick and vomited. He suffered more or less constantly from flatulent dyspepsia. His mother had died of angina pectoris at 66; his father of bradycardia at 76. He had four healthy children. The Wassermann reaction had always been negative; both the blood and cerebro-spinal fluid were recently tested. There was, however, some slight involvement of the nervous system: the knee-jerks were sluggish; the abdominal reflexes absent; the pupils were equal, of average size, but sluggish to light and on accommodation. His pulse rate was 56 per minute; blood pressure —systolic 120, diastolic 75. The urine was normal. On one occasion definite tenderness and rigidity were present in the right upper quadrant of the abdomen. X-ray findings were negative, although the radiologist considered there might be some thickening of the gall-bladder.

In this case one felt that there was some myocardial degeneration which was secondary to an abdominal condition, either chronic gall-bladder or pyloric ulcer—the therapeutic test of belladonna supported this view, as 5 minims of the tincture acted like a charm in removing the gastric discomfort and also in relieving the chest and arm pains. Alkalis had no effect, and this, in my opinion, rather favoured the diagnosis of gall-bladder trouble. For a time with belladonna, the patient was able to carry on, but then symptoms of glaucoma occurred, and with the stopping of the belladonna the abdominal symptoms increased in severity. The tenderness on pressure over the gall-bladder returned and also Ligat's reflex was positive, so an operation was decided upon. At this stage an electrocardiogram showed an inverted T-wave and the cardiologist gave a bad prognosis. However, the patient's life was intolerable, so the operation was performed. At the operation the gall-bladder was found distended and adhesions were present round the cystic duct. The duodenum and other organs were normal. The gall-bladder and appendix were removed. The patient made a good recovery; all his symptoms were relieved, although on exertion he suffered from tightness in the chest amounting at times to pain. A subsequent electrocardiogram did not show the inverted T-wave. It is now 2½ years ago, and he is in a better condition than previous to the operation.

It might be asked, why so long in deciding upon an operation, and why not have done an exploratory laparotomy? The reasons were: (1) the patient's history was unsatisfactory; (2) with an impaired myocardium an exploratory operation was not justified; (3) as soon as Ligat's reflex was positive over the gall-bladder, one felt it was diseased and that an operation appeared the only means by which the patient could receive any relief.

The findings in certain conditions may be negative or difficult to interpret: (1) Cases of general peritonitis with abdominal distension. In doing the test one must avoid the slightest pressure on the abdominal wall. (2) Neurotic patients, especially when there is a genuine lesion. (3) Cases where there is local inflammatory œdema of the abdominal wall. (4) Cases of hypothyroidism and panniculitis, as pain is complained of whenever any part of the skin and subcutaneous tissue is pinched. Even in these cases, when an organ is diseased, the response is more intense over the corresponding hyperalgesic area. To clinch the diagnosis of hypothyroidism, I examine the inner side of the knee and thigh immediately above, where the peculiar appearance of the skin and the tenderness on pinching it and the subcutaneous tissue are most easily demonstrated. (5) Cases of tuberculosis involving the cæcal area. (6) Cases where the organ is diseased, but the reflex absent. Ligat states: "I should never hesitate to operate on a case which gave the ordinary clinical signs of an acute appendix, although I failed to elicit a reflex, nor should I be prevented from opening an upper abdomen in a case which, although it gave me no gastric reflex, presented the usual signs of a perforated stomach or duodenum." He came to the conclusion that in some cases of appendicitis, the failure to find hyperalgesia was probably due to blocking of the afferent impulses at the mesentery of the appendix on account of its gangrenous or thrombosed condition. In other cases he could find no reason at all.

I have found the reflex valuable in gastric or duodenal conditions, gall-bladder disease, appendix trouble and certain conditions of the large bowel, such as diverticulitis and ulcerative colitis, and also in tubal disease. The following case exemplifies its use in a case of duodenal ulcer :—

I was called up one night at 2 a.m. to see a man, aged 56, who was suffering with acute abdominal pain in the epigastrium. Rigidity in the right rectus was present and Ligat's reflex positive over the duodenal area. An acute duodenal ulcer with slight perforation was diagnosed, and a surgeon who saw the patient the following morning agreed with the diagnosis. An operation was advised in view of the urgency of the symptoms, but the patient decided to wait. With rest in bed, diet and alkalis the patient recovered. Two years later, persistent indigestion symptoms with pain in the appendix area and the presence of Ligat's reflex in the area necessitated an operation. A small piece of shot was found in the appendix and the duodenum showed the scar of a healed ulcer.

The following case was treated as suffering from duodenal ulcer until the appendix proved to be the seat of the trouble :—

A man, aged 25, eight years previously had occasional attacks of gnawing pain in the epigastrium, which commenced 2 to 2½ hours after meals, and was made easier or disappeared on taking food. At this time the attacks usually came on during the winter months, and the patient thought they were due to a " chill." Four years ago, the attacks became more frequent, and whilst the pain came on in the epigastrium 2 to 2½ hours after meals, it would settle down to the lower half of the abdomen, but not to the right side. The attacks would also waken him at night. Taking food usually relieved the pain and also, during the attacks the bowels were at times loose. Subsequently the attacks became more frequent, and severer, and in July 1932, whilst he was working in London, the pain was more or less continuous all the day, and was not relieved by taking food. From the commencement of his illness, he only vomited twice. He attended the out-patient department of a general hospital in London, and on July 21, after an X-ray examination, a diagnosis of duodenal ulcer was made. On August 24 he was admitted as an in-patient and discharged after three weeks with instructions to continue strict dieting under medical supervision at home. When examined on September 16, Ligat's reflex was positive over the duodenal area, and tenderness was present on deep pressure over the outer border of the right rectus slightly above the level of the umbilicus; no reflex or tenderness was present over the appendix or other areas. He was gradually improving when, on October 7 for the first time, he complained of pain in the right iliac region; tenderness was present on deep pressure in this region and the appendix reflex was positive.

While waiting to be admitted into the Harrogate Infirmary the duodenal reflex became negative, and his condition generally improved. The abdomen was explored on November 22, when the surgeon reported as follows: "There were some adhesions between the gall-bladder and transverse colon, but no sign of a duodenal ulcer. His appendix contained a stercolith over an inch long, and this was probably the cause of his abdominal pain." In this case, one feels that the duodenal symptoms were secondary to the appendix and may have been produced by hyperchlorhydria. With a short history, one might have considered the possibility of an ulcer having healed without showing any naked-eye signs, but with a history of eight years, one would expect a scar or thickening to be noticed at the operation.

When treating a duodenal or gastric ulcer medically, it is helpful to use Ligat's reflex as a guide to the progress of the case; if healing is taking place the reflex gradually disappears. In cases of suspected gall-bladder disease, if Ligat's reflex is present only over the gall-bladder region, sulphur waters internally and the application of liver packs relieve the symptoms in the majority of cases.

In one family at different times, I had as patients two brothers and a sister, ages 44, 42, and 36, with acute cholecystitis—*Ligat's reflex being positive*—all of whom cleared up on removal of teeth with an apical infection, and there has been no recurrence of the inflammation in any one of them. The presence of Ligat's reflex is of undoubted value in cases of appendix disease. In cases of recurring dyspepsia with indefinite symptoms, without pain or tenderness over the appendix, but a positive reflex, it is safe to advise the removal of the appendix with advantage. Occasionally with prolonged appendix dyspepsia, a dilatation of the stomach occurs and this requires treatment after the removal of the appendix; it is therefore my practice where the reflex is positive to advise early removal.

The presence of the reflex is most helpful in cases where the appendix is not in its normal position—pelvic or retrocæcal, as without this sign the diagnosis would be difficult. Ligat had one case with a positive reflex where the appendix at the operation was found on the left side of the abdomen. In infants and children it is equally helpful.

In a baby, aged 9 months, who had attacks of vomiting and "crying fits," the reflex was present, and after the removal of the appendix there was no further trouble.

When my daughter was four years old, she wakened up one night about 12 midnight with severe vomiting, but no localizing pain or tenderness over the appendix. She had had one similar attack previously when I had not the opportunity of examining. The appendix reflex was present, and Mr. Frankling kindly removed a diseased appendix the following week. She is now 14 and she has had no further trouble.

A child, age 12, with no localizing symptoms, on examination the only physical sign was the presence of the reflex. I advised appendicectomy A surgeon was consulted, but did not advise the operation then Two years later, while she was at a boarding-school, she had a definite attack of appendicitis and the appendix was removed

Occasionally after an operation for appendix abscess, the stump of the appendix gives rise to trouble later.

A male patient, aged 40, gave a history of having an abscess opened and the appendix removed 1½ years previous to my seeing him. The surgeon who had operated corroborated this. On and off he had suffered from indigestion since and at times pain in the right iliac region. Ligat's reflex was present over the appendix area After removal of the appendix stump the patient had no further trouble.

Sometimes it is very difficult and impossible to say whether one is dealing with appendicitis or inflammation of the right tube and ovary; or if both are involved which is the organ primarily at fault. In this class of case, Ligat's reflex can be very helpful.

A married woman, aged 39, had two children, aged 17 and 14, and had enjoyed good health. The periods had always been regular, of five days' duration, and not excessive. The period previous to my being called in had suddenly stopped on the third day, and the patient wondered whether she might have contracted a chill. About the time the next period was due, she experienced severe pains in the lumbar region of the back, which in six hours' time affected also the lower half of the abdomen, about the umbilicus, and to the right side chiefly. The pains were colicky in nature, and frequent vomiting occurred, even after drinking water. When examined at 9.30 p.m., slight rigidity was present in the lower half of the right rectus. Ligat's reflex was absent over the appendix area, but present over the tubal area. Her temperature and pulse-rate were normal. Next morning the temperature was 99·5; pulse-rate 84; tongue very furred; no flatus had been passed downwards and the vomiting had persisted through the night. Tenderness over the right iliac region was marked. Ligat's reflex was markedly present over the tubal area. Per vaginam, a degree of tenderness was present in the right fornix; the uterus was movable, but pain was elicited when it was pushed over to the right side. In the evening the temperature was 99°, pulse-rate 80. Less pain was complained of and there was less sickness. A degree of rigidity was still present over the right rectus below the umbilicus; pain also was present on pressure over the right iliac region; Ligat's reflex was now present over both the appendix and tubal areas, but was more marked over the tubal one. The following morning there was an all-round improvement, only very slight tenderness and rigidity being present; flatus had been passed downwards; the appendix reflex was slightly positive; the tubal one was more marked, but definitely less. On the fourth day menstruation commenced, and she was decidedly better. This case had all the appearance of an acute abdomen at first, and if I had not had the help of Ligat's reflex, I should have pressed for a laparotomy.

The reflex is present in cases of ulcerative colitis and diverticulitis, but I have not found it present in all cases of cancer of the large bowel. In one case in which the appendix reflex was positive, and the large bowel reflex negative, the operation revealed a diseased appendix and an inoperable cancer of the pelvic colon. Fortunately this combination is not common. It is, however, necessary always to take as broad a view of a case as possible, remembering that even if Ligat's reflex is positive, showing disease in any organ, this particular organ may not be giving rise to any of the symptoms the patient complains of. The following case of subacute combined degeneration exemplifies this:—

A man, aged 61, gave a history of having broken down in health three years previously. Eighteen months later the appendix was removed, but with no appreciable improvement. During the last twelve months he had lost one stone in weight; he was soon tired, complained of tingling sensations in the hands and arms, of chilly feelings in the body and a loss of grip in the hands and no feeling in the fingers, having difficulty in picking up a coin off the table. A slight icteric tinge was present in the face; the systolic blood pressure was 110, and the diastolic 75; the muscles of the hands and arms were wasted; the vibratory sense was practically absent below the knees and diminished in the upper extremities; the skin sensations appeared normal. The liver was palpable half-an-inch below the costal margin and was tender on pressure. Ligat's reflex was markedly positive over the gall-bladder area. I formed the opinion the patient was suffering from peripheral neuritis and chronic cholecystitis, the gall-bladder probably being small, contracted and thickened. The drinking water was examined for lead and none found, so I considered the neuritis was the result of toxins arising from an infected gall-bladder. An attempt was made to X-ray the gall-bladder on two occasions, but unsuccessfully, as on each occasion he immediately vomited the capsule taken for the purpose of cholecystography. Various treatments were given for the gall-bladder, and an operation was even suggested. After the patient returned home, another doctor diagnosed the condition, gave him liver internally, and marked improvement occurred. While this patient may have had cholecystitis, there is no doubt he had pernicious anæmia, which I failed to diagnose.

In many abdominal conditions the absence of Ligat's reflex is very helpful, such as the following: cardiovascular, chest or renal diseases causing abdominal symptoms; gastric crisis of locomotor ataxia; streptococcal infection of the bowel secondary to infected teeth. The protean symptoms in the latter condition may be very puzzling.

A man, aged 58, four years previously had symptoms of a duodenal ulcer which cleared up after treatment, and later some infected teeth were removed. He now complained that for some time he had been easily tired; having no appetite; suffering pains at times in the right side of the abdomen or across the epigastrium; the motions being liquid and watery. There had not been any loss of weight; the tongue was furred and rather dry; the complexion sallow. Systolic blood pressure was 115, diastolic 75. Tenderness on deep pressure was present over the right iliac region and also over the right rectus above the umbilicus. No Ligat's reflex was present. The remaining teeth were infected, and after removal the symptoms gradually cleared.

A similar case in a woman, aged 49, was more difficult to treat as she preferred an abdominal operation to losing her septic teeth, and in this attitude she was backed up by her husband. A noted surgeon had removed her appendix five years previously. A gynæcologist had about the same time treated her for endometritis. No treatment, however, had affected her symptoms of lassitude, indefinite indigestion with abdominal pains and continuous loss from the uterus of a blood-stained slimy discharge. Some of the most infected teeth were removed with a decided improvement following. Nothing would induce the patient to have a clearance of the mouth, although she would have been willing to have the uterus removed, if this course had been advised.

Another class of case which is frequently operated upon without benefit is that of abdominal neurosis.

A patient of mine, aged 40, a doctor's wife, had been operated on three years previously and all the abdominal organs had been found normal, including the appendix, which was, however, removed. In one attack I saw, she had the appearance of an acute abdomen —the face was pinched and blanched with a very anxious look; acute pain was complained of across the upper half of the abdomen; the pulse could not be felt at the wrist; the muscles of the abdomen were held rigid. Ligat's reflex negative. The history of the operation for a similar attack influenced me in not sending for a surgeon for his opinion. When the patient came round she had diarrhœa, passing a watery motion with mucus but no blood. Subsequently a strong neurotic element was found in this case, and she stated that from childhood she had always experienced an intense fear when left alone.

The absence of Ligat's reflex is also useful in cases of pyloric obstruction without an organic lesion. Such cases are occasionally met with in highly-sensitive people.

A man, aged 68 years, of a highly nervous temperament, periodically for years had had acute abdominal attacks lasting for weeks. During the attacks he was doubled up with acute pain in the epigastrium, and vomiting occurred immediately after taking any food. Ligat's reflex was not elicited. Seven years previously a normal appendix had been removed. X-rays on two occasions showed no abnormality. When I first saw him, two years ago, the attack had been almost continuous for two months. His weight had gone down from 10 stones 6 lbs. to 7 stones 1 lb. A surgeon saw him in consultation, and we both feared he was suffering from inoperable carcinoma. After overtiring himself physically, he had an attack a year later, and this quickly responded to belladonna in 5 to 10 minim doses and alkalis. He has recently recovered from a rather severe bout following an attack of lumbago. This time he was ill in bed for two weeks.

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DIPHTHERIA IMMUNIZATION IN INFANCY

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DURING the course of the most recent sustained campaign against diphtheria in New York City, opened in January 1929, up to the close of last year, the 4 years' efforts—organized and co-ordinated in the completest possible manner by combination of public health authority, private practitioner, nursing and health visiting activity—had resulted in a total of over 680,000 children being immunized (irrespective of those dealt with in previous campaigns, dating back to 1918). Of that number, 40 per cent. were dealt with at Health Department Stations (child welfare centres), 32 per cent. in schools, and no less than 28 per cent., or nearly 190,000 children, immunized by private practitioners. During the period since 1929, there has been a weekly average not far short of 3,500 children treated.

As compared with such totals, London figures of the numbers immunized or known to be immune as Schick-negative, since work was begun at the welfare centres of twelve Metropolitan boroughs, appear insignificant, amounting only to about 18,000 (or 1·9 per cent. of the London child population under 15) at the end of 1932. Of that total, roughly 40 per cent., or 7,000 only were of pre-school age, under 3 per cent. of the 0 to 5 population. In Birmingham, with a quarter of London's population, by public health and school medical co-operation since 1925 a total of about 50,000 pre-school and school-age children have been immunized or known to be Schick-negative, under one-fifth of that total being from 0 to 5 years, or about 10 per cent. of the pre-school age population. Of the New York total of 633,000 immunized up to July 1932 or 40 per cent. of the population under 15, over 170,000 (or 27 per cent.)

were children under 2 years, and 230,000 were under 6 years, representing a proportion of 36 per cent. protected among the pre-school age population of 635,000.[1]

The recent work of E. S. Godfrey[2] on the results of immunization carried out in New York State, described in his paper at Montreal over a year ago, has demonstrated the importance of immunization among infants in the first five years of life before any real effect can be produced on the general diphtheria rate, in spite of the immunization of large numbers of children of school age. From a number of examples which Godfrey quotes of preventive inoculation in populous centres (of half a million to 30,000 population) in New York State, it seems evident that although 50 to 70 per cent. of children of school age had been protected, it was not until at least an additional 30 per cent. or more of those under 5 years had been immunized that any fall in the diphtheria rate of the community as a whole was produced. It is perhaps no less significant that in New York City with the increasing proportion of immunized children under 6 years, amounting to 36 per cent. at the end of June 1932, there has been the striking decline in diphtheria incidence and mortality since 1928, from 10,776 cases and 642 deaths, to 3,585 cases and 212 deaths in 1932, the lowest case record yet reached.

It is clear that wherever immunization work is being conducted, efforts should be concentrated on urging the protection of the pre-school child who is exposed to greater risk from his higher susceptibility and from home contact with older children attending school. As example of such effort to induce parents to get their younger children protected, I would refer to the measures adopted in Beckenham by Dr. Philips Cole, since 1930.[9] In the infants' departments of five Beckenham schools it was found that the proportion of immunized to new admissions averaged only 30 per cent., which was regarded as insufficient to maintain the desired degree of mass immunity. To stimulate interest, therefore, charts were prepared for each classroom of the five infants' departments showing the degree of protection which had been reached in the different classes, with an arbitrary line about two-thirds of the way up, or 60 per cent., to indicate the supposed danger zone. At the end of 1931 only one out of 18 infant classes had been sufficiently protected as to be above that safety limit, and every effort was to be made in 1932 to bring the immunity in other classes out of the danger zone. Dr. Cole has also observed the significant fact that the waves of increased diphtheria prevalence have apparently succeeded each other at intervals closely corresponding to the period elapsing between earliest school entry to the infants' department and the later transfer to the senior department, roughly five or six years, during which it may be presumed the proportion of susceptibility increases with each new batch of entrants, until in course of time, the transfer of the older, more immune children to the senior department had sufficiently lowered the herd immunity of the remainder to allow of epidemic outbreak.

With regard to the mortality from diphtheria during the years of infancy, 0 to 5, in 1930, in all England and Wales, there were 126 deaths among infants under 1 year, representing 20·6 per 100,000; in London there were 29 deaths, or 44 per 100,000 under 1 year. Among the children aged 0 to 5, 1,473 deaths were reported in the whole country, or 48·3 per 100,000 in that age group, as compared with under 1,800 deaths at the school ages of 5 to 15 years, or 27·4 per 100,000 in that 10 years' age period. In London 257 children under 5 years died of diphtheria, representing 76·5 per 100,000 of pre-school age, whilst 176 deaths were recorded among those of school age—a proportion of 26 per 100,000 at 5 to 15 years. In London, therefore, the mortality rate from diphtheria under 1 year was more than double, and at 0 to 5 was nearly double that in the whole country, whereas in the years of school life, 5 to 15, the rates in London and England and Wales were practically the same. Hence the need for the protection of the pre-school child in London.

At how early an age should immunization be carried out? Monrad[3] in Denmark has questioned the correctness of the general procedure advocated or observed in delaying immunization until the second year of life, on the ground that he had found the supposed maternal transmitted immunity in infants to vary considerably during the first twelve months of life. Thus, among 29 of under 1 year, 21 were Schick-positive, 15 of them being bottle-fed and 6 breast-fed infants, and of the 8 Schick-negatives, 5 were bottle-fed and only 3 breast-fed; also among 12 infants of 2 to 6 months, 6 were Schick-negative and 6 were positive reactors. In Italy, Schwarz[4] has recorded attempts to immunize newborn infants and nurslings. One group of 11 months to 2 years was given 3 injections of toxoid, and in another group of 10 newborn infants, each received two injections of 0·5 c.cm. T.A.T. floccules. Subsequent Schick testing and estimation of the antitoxin blood-content of the two groups showed that those under 6 months failed to produce antitoxin; its absence was attributed to a condition of specific inertia preventing reaction to diphtheria antigens and to the want of stimulus to provoke the formation of antitoxin. Schwarz was also of opinion that owing to lack of sensitiveness of the skin in infants, a negative result to the Schick test was no indication of their immunity. Hence he maintained their need of passive immunization with antitoxin inoculation, if exposed to risk of infection.

Okell[5] in his second Milroy lecture referred to his joint observations with Glenny and Maizell on the Schick testing of 37 children aged 3 weeks to 6 months, only two of whom proved Schick-positive; but 29 out of the 35 Schick-negatives had less than 1/500 unit of antitoxin per c.cm. of their blood, and 21 had only

1/1000 of a unit or less. Therefore the failure of infants to react to the Schick test is not necessarily associated with the presence of circulating antitoxin. Okell also noted that the lack of data for determining if the non-reactivity of the skin is associated with a general insusceptibility to the toxin; and for explaining how the universal acquirement of sensitiveness to diphtheria toxin comes about during the first and usually most sheltered months of infant life. W. H. Park[6] has emphasized the importance of immunizing infants as soon after the age of 6 months as possible, and certainly before the first year, owing to the increasing mortality from diphtheria, with age, after 6 months up to the second and third year of life.

The results of these several observations, which throw doubt on the wisdom of postponing immunization until the second year, seem to suggest that inoculation should preferably be carried out during the second six months of infancy, especially in the case of those exposed to risk of infection from home contact with brothers or sisters attending school. It must, at any rate, be regarded as admitting of no dispute, that the chief aim in this work of diphtheria prevention is to educate parents to appreciate the necessity of securing protection for their children during the first years before entry to school, and the earlier the better. As a further means of approach, wider use should be made of the system, too little applied in England, of informing parents, at the birth of each child, of the need for its protection against diphtheria after the age of 6 months, when a second energetic reminder should follow with a call by the health visitor.

It is equally important that every encouragement and opportunity should be afforded to enlist the general practitioner to take a far more prominent part in advocating immunization to his patients, and, indeed, to carry out the work himself as readily as the administration of any other subcutaneous injection. He would indeed be pursuing the path in preventive medicine, which, as Sir George Newman but lately emphasized,[7] the private practitioner has a right, if not bounden duty, to follow. Hitherto, his part in this branch of preventive medicine, certainly in this country, has been almost entirely negative, in marked contrast to the important share in New York of the practising physicians, in the campaign still steadily going on, by their immunization of over 180,000 children.

With reference to the general practitioner's attitude over here, a comment was recently made, that the average medical man in practice knows little or nothing of the Schick test. If such is really a fact, while that state of ignoring the means of prevention persists, so long will diphtheria continue to levy its heavy toll. One hopes that at the present day, no medical student will be able to qualify without that very indispensable knowledge of so important a branch of preventive medicine; for the practical applications of the Schick and Dick tests and of immunization against diphtheria and scarlet fever should of necessity be included, as essential to the medical curriculum. It is, however, encouraging to find from recent annual reports of medical officers of health that, in some of the large towns, where immunization clinics have been opened, practitioners in private practice are taking an active part in the work of diphtheria prevention. Thus, in Liverpool, out of a total of nearly 1,600 persons immunized in 1931, over 200 had been inoculated by general practitioners.

A final word bearing on the contrast of the hold which the adoption of immunization has taken in America and elsewhere, as compared with its minor prominence in this country. No real progress can be expected until there exists between all those already responsible for much individual effort, a closer co-operation and combination in a concerted endeavour to secure adequate propaganda work, both for the more general adoption of preventive inoculation, and for gaining the confidence and active support of the medical men in general practice. It is encouraging to know that the nucleus of such a body has been formed at the Ministry of Health[8]—one welcomes the news of its formation, as well as the decided verdict in 1931 of the League of Nations Committee of Experts on the value of immunization. But more than that is needed. It is no doubt true that we do not possess or make use of such driving power or means of publicity as are so prominent a feature of public health activities in the United States; nor have we at our disposal such necessary funds as have been so freely provided for the past three years' campaign in New York, where the Milbank Memorial Trust and the Metropolitan Life Insurance Company shared in defraying half the cost of 140,000 dollars (about £35,000) annually expended in the great effort to combat diphtheria. From the apparent results there is little doubt it has been money well spent. May not we in London hope for a similar combination and organization, with the backing of the business interests and financial aid of some corresponding insurance firm and trust body? The course of events may urgently call for answer to such an appeal.

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THE PRESENT POSITION OF MANIPULATIVE SURGERY

By PHILIP WILES, M.S., F.R.C.S.

MANIPULATIVE surgery is a practice which is often regarded as being exclusively in the hands of unqualified practitioners. Of recent years, however, there has been a change in the attitude of our profession so that, sifting the good from the bad, it has been possible greatly to enlarge the scope of this work and add it to the common stock of medical knowledge. There are many gross conditions which obviously require manipulative treatment, but there are also a large number of minor cases of pain associated with the function of joints and muscles in which this line of treatment is not so apparent. The latter complaints, although not serious in themselves, may cause great distress by their constant pain, and unless their true nature is understood they cannot be treated satisfactorily. It is these that are being considered here as they mostly respond well to manipulation.

The actual lesion in the majority of such cases is not, as one so often hears, " a bone out of place." The trouble is really the end-result of some strain or misuse of the affected part which injures the ligaments surrounding a joint or the tendinous insertion of the neighbouring muscles. The injury is healed by a scar, which in this situation is called an " adhesion," and pain is caused by every movement which stretches the adhesion. By manipulation the adhesion is broken and the pain is relieved. A small proportion of cases are of a different nature as they are of abrupt onset and therefore there can have been no time for adhesion formation. An example of such a case is the man who suddenly finds his wrist locked in the dorsiflexed position whilst making a stroke at golf. What has occurred is probably in the nature of a "seize up." The lubricating synovial fluid has been squeezed from between the opposing joint surfaces which consequently only require separating by manipulation to effect a cure.

THE BACK

CHRONIC BACK STRAIN.—Chronic pain in the back is a common complaint which includes a number of clinical and pathological conditions. We are now concerned only with those cases which have an etiology on the lines described and which are conveniently termed "chronic back strain." The condition is much more common in women than in men and the lumbar and lumbo-sacral regions are those chiefly affected. Possibly the sex incidence and the lumbar localization are connected, at any rate to some extent, with the fact that the forward tilt of the pelvis and therefore the curve of the lumbar spine are greater in women than in men.

Bankart has divided cases of chronic back strain into three types, sacro-iliac, lumbo-sacral, and lumbar back strain. If to these are added dorsal back strain, the classification will be found very useful in deciding on treatment and assessing prognosis (Fig. 1). It will often be found, however, that although the maximum point of pain and tenderness is localized to one of these areas, an additional pain, widespread over the back, is present as well. This pain is characterized by its lack of precise localization and by its variability in position from minute to minute. It must be regarded as "functional" in nature as it disappears immediately the primary disorder is cured.

Sacro-iliac strain is the most typical form of chronic back strain and also the most satisfactory to treat. It arises in the great mass of muscles and strong ligaments which suspend the sacrum from the ilium and transmit the whole weight of the body to the lower limbs. They are in constant action in both sitting and standing positions, so that any disorder

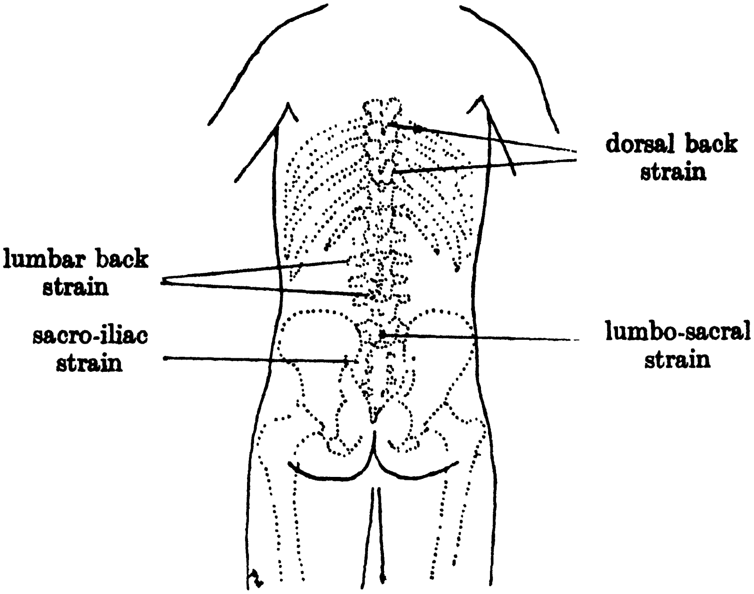

FIGURE 1.

of them causes continuous pain and is most disabling. In these cases pain is complained of at the bottom of the back; it may be worse when standing or lying down, according to the precise part of the joint affected. Thus an adhesion at one spot is stretched when standing, whilst at another spot it is stretched when there is lateral strain on the joint, as when lying on a soft bed. On examination, pain and tenderness are accurately localized to a point just internal to the posterior superior spine of the ilium. The patient must be made to identify this spot with the tip of one finger; a sweeping gesture of the whole hand will not suffice. The symptom is pathognomonic of sacro-iliac disease, but an X-ray must invariably be taken to make certain that the disease is not tuberculous.

Lumbo-sacral strain arises in the articulations between the sacrum and the fifth lumbar vertebra. The upper surface of the sacrum slopes downwards to form an angle of about 50 deg. with the horizontal, so there is a tendency for this vertebra to slide forwards off the sacrum. For this reason it is more subject to strain than the other lumbar joints. Pain and tenderness are localized over the spine of the fifth lumbar vertebra with nearly as great precision as is the localization in sacro-iliac strain. Manipulation in cases of lumbosacral strain, however, does not give such uniformly good results. The articulation is a complex one with extensive movements, and it is almost impossible to fix the bones on either side of it so that the full range of movements can be secured. Nevertheless, it is always worth while to try manipulation, especially in thin patients, as a certain number can thus be cured, and the only alternative is operation.

Lumbar back strain is a less easily defined entity. It is due to disorder of any of the joints of the lumbar vertebræ or to strain of the insertion of the muscles into the transverse processes of the vertebræ. Localization of pain may consequently be almost anywhere in the lumbar region, although it is perhaps commonest over the tips of the transverse processes. On the whole manipulation gives good results.

Dorsal back strain is the least common of all, but it does occur from strain of any of the costo-vertebral, costo-transverse or intervertebral joints or any of the muscles inserted into the ribs and vertebræ. The symptoms are similar to those in cases of low back strain with the exception that pain is sometimes referred along an intercostal nerve; this is most likely to occur when a costo-vertebral joint is affected. In all cases of intercostal neuralgia in which a cause cannot be found it is worth while to try manipulation.

Treatment.—The treatment of chronic back strain is mobilization by manipulation. To place such a case in a cumbersome support merely aggravates the trouble. Pain is only partially relieved by the support whilst its additional weight makes more strain. Sacro-iliac strain of recent onset in a patient who is not too fat can often be manipulated without an anæsthetic. For the rest a general anæsthetic is required to give complete muscular relaxation. A warning is necessary that no back should be manipulated until after it has been X-rayed. It is sometimes impossible to tell by clinical examination the nature of the underlying disease, and if this precaution is neglected disaster is sooner or later bound to follow.

The technique of the manipulation of the sacro-iliac joint is of sufficient interest to describe in detail. To manipulate the left side the patient is placed lying on the right side near to and facing the edge of the table. The left leg is allowed to hang over the table and is steadied between the operator's legs. The right arm is placed forwards and the left backwards, so that the body is twisted. The operator grasps the patient's left arm near the shoulder with his left hand and his right arm lies along the crest of the ilium, so that his elbow is over the sacro-iliac joint. Now with a rotary movement the patient's left arm is forced backwards and the pelvis forwards and downwards, so that the trunk is twisted and the ilium is rotated about the sacrum.

Rest in bed is not usually necessary after a spinal manipulation. If the case is a severe one a masseuse should start at once and heavy, deep work is required. A ladylike touch is no use at all. Exercises on ordinary Swedish lines should be carried out daily for about a month to ensure that mobility is maintained.

ACUTE PAINFUL BACK.—This when not due to gross disease or injury, is of two main types. The one follows trauma or an obvious strain, and if left alone may be expected to develop into chronic back strain. It responds excellently to immediate manipulation during the acute stage. The other type includes acute lumbago and acute " stiff neck." These two are grouped together without any real knowledge of the pathology of either because they are clinically similar and respond to the same treatment.

Acute lumbago presents a picture so well-known that it is unnecessary to describe it. It is a condition which it has been customary for many years to treat with morphia and prolonged rest in bed. Nothing else, it was said, could do it any good, yet the effect of manipulation is sometimes so startling that one wonders how it came to be overlooked. Without an anæsthetic and with exceeding gentleness it is possible to move the patient from the acutely painful arc in which he has been fixed. A little perseverance and he will have acquired quite a good range of free movement. I have seen a man who was curled up in bed with lumbago walking about the room in half an hour. It is true he was not completely free from pain, but at any rate he was able to go about his work.

Acute stiff neck is another well-known and painful clinical entity. It responds to a few days spent in bed and the application of antiphlogistine. This waste of time is usually unnecessary. If the neck is manipulated under simple gas anæsthesia, as often as not the pain goes immediately. It can even be done without any anæsthetic at all.

THE FEET

A foot has to do a very great deal of work and has to absorb a considerable shock every time a step is taken. It is strongly built to meet this strain and, whilst its mechanism is in good working order, it is quite equal to the job. The " spring " in the foot is provided by the muscles—not by the ligaments, and it is the muscles also which are responsible for the normal posture of the foot. The normal function of the ligaments around the joints of the foot, as of most other joints, is not to maintain posture but to limit the extremes of the range of movements. The tone of the muscles is therefore of prime importance. Immediately it is lost the ligaments are called upon to maintain posture and are subjected to an unaccustomed strain; this injures the ligaments and gives rise to adhesion formation. This and allied conditions it is convenient to group together for clinical purposes as "foot strain." Only adults will be considered here, however, because children present rather different problems. The shape of the foot, whether it is long, thin, high-arched or flat (excepting extreme degrees of this latter), does not matter in the least; if the foot and its muscles are functioning properly it will be painless. Painful feet, in whatever type of foot, can be divided clinically into three groups—foot strain, arthritis, and gross deformities. The latter are not here of direct concern.

Foot strain has the following as its most common precipitating causes in approximately their order of frequency, and they are all referable to the action of the muscles : (1) standing for long periods; (2) walking or working on rough ground; (3) minor deformities, such as corns, causing faulty use of the foot to avoid pain; (4) external trauma, e.g. a weight falling on the foot; (5) excessive weight; (6) athletic games and toe-dancing; (7) systemic illness causing a long stay in bed. Foot strain is therefore not confined to any class of patient, but includes every possible walk of life.

The clinical picture varies with the affected joints and the duration of symptoms. In the early stages complaint is made of acute pain which can be accurately located by the patient. As time passes there arises also a general aching which may eventually spread over the entire foot and up the leg. There is also present very frequently a greater or lesser degree of swelling of the foot and ankle. The swelling is a superficial œdema which may accompany any disorder of the foot. This and the widespread aching must not be allowed to obscure the diagnosis; they are often mistaken for signs of rheumatism and treated with salicylates.

There are five common sites to which pain is referred : the inner border of the foot, under the outer side of the ball of the foot, below and in front of either malleolus and what the patient describes as "inside the ankle." When the foot is examined each group of joints is separately put through its full range of movements. As a rule the pain of which the patient complains will be produced by the extreme of one of these movements. Some feet are very stiff and almost anything hurts. Others are so supple that it is hard to see where there is any limitation of movement, but careful examination will usually reveal the affected spot. An X-rays should be taken whenever possible to exclude other disease.

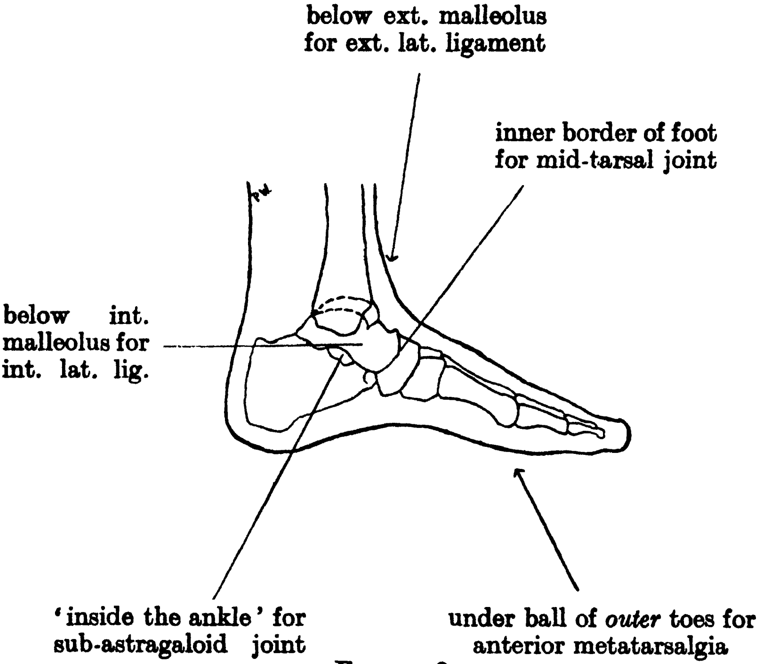

FIGURE 2.

The inner border of the foot is the most typical site of pain. Such patients almost invariably complain that "their arch has dropped," and as often as not have tried arch-supports. Flat foot has nothing whatever to do with painful foot, and people with flat feet are even less likely to suffer from painful foot strain than those with medium or high arched feet. The harm caused by the prolonged use of arch-supports in these cases cannot be exaggerated because they prevent the natural movements of the foot and thus encourage further stiffening. The relief obtained is therefore only temporary and the condition becomes harder and harder to treat.

Anterior metatarsalgia is pain situated under the outer side of the ball of the foot, that is under the heads of the outer metatarsals. Bankart has pointed out that the first metatarsal is made large and strong, compared with the other metatarsals, for the purpose of carrying the body-weight. If the foot is wrongly used so that the weight falls to too great an extent on the slender outer metatarsals, they are very likely to give way under the strain. This is so constant a cause of pain at this site that one knows before looking that the shoes will be found to be worn much harder on the outer than on the inner sides.

Pain just in front of and below either malleolus is due to strain of one of the lateral ligaments of the ankle joint, i.e. the deltoid and external lateral ligaments. The patient also points to one of these sites when the astragalo-calcanean interosseous ligament and the sub-astragaloid joints are involved, but he then describes the pain as being " inside the ankle " instead of being superficial. It is necessary to distinguish between these types because they call for different movements when the foot is manipulated.

Treatment.—The treatment of foot strain is manipulation. The amount of force used is the subject of much variation. Most bone-setters are limited in the amount of force by the absence of an anæsthetic, but it is noteworthy that one of the most successful of them made great use of anæsthesia. Some surgeons, on the contrary, use all their strength. A middle course, one which varies with the type of case, seems to me the best. The minor case with a supple foot can often be treated without an anæsthetic. In more severe cases an anæsthetic is essential for really good results. Very stiff feet should not be mobilized at one sitting as the reaction and bruising are so severe that the patient is unable to maintain the correction. It is a much better practice to repeat the manipulation two, three, or even four times, so that the improvement gained at each stage is permanent.

After-treatment, in all but the slightest cases, is so important that it should be regarded as part of the treatment rather than as an accessory to it. It consists of exercises which should become part of the daily routine until the trouble is over. The exercises are specially designed to maintain movement and also, even more important, to strengthen the intrinsic muscles of the foot. In the more severe cases a few days' rest in bed is desirable and a masseuse should get to work later on the day of the manipulation. A " follow-up " I am making suggests at first sight that it is the younger patients who give the most gratifying results, but this is only because the incidence of arthritis is so much higher amongst older people. One of the most striking results was in a lady of 64.

Arthritis as a cause of painful feet is rather a different problem. Osteo-arthritis is common and is traumatic in origin from the constant hard work of the feet. Rheumatoid arthritis is hardly less often seen, and many cases are of gonococcal or other known bacterial nature. The joint surfaces may be more or less destroyed and the entire ligamentous structures infiltrated and thickened by inflammatory changes. The feet are usually very stiff and pain is widespread. X-rays often show bony changes.

There are two lines of treatment available and they can often be combined with advantage. Shoes may be made to fit the foot accurately and give it even support. It is no use just putting in stock-size arch-supports; very careful fitting of the whole shoe is necessary. In addition, the foot may in some cases be mobilized, but on no account must any joint be manipulated until the acute stage of the disease is over. If mobilization is decided upon the greatest care must be exercised over the amount of force used so as to avoid damage to the contracted ligaments; the object is to stretch them so that the joint surfaces are less crowded together. Each case presents an individual problem which must be settled on its own merits, and with judicious handling most patients can be kept comparatively comfortable.

THE KNEE

The knee joint is situated, from a mechanical point of view, in a difficult situation because it has to have a wide range of movement for the purpose of locomotion and yet stability is essential. When one thinks of the enormous leverage of the two long bones forming the joint it seems remarkable that injury is not even more common than it is. The stability of the joint is provided by the muscles and tendons which surround it on every side; the extremes of movement are limited laterally by the lateral ligaments, and in an antero-posterior direction (as distinct from flexion) by the cruciate ligaments.

Of the many types of derangement of the knee there are two in which manipulation plays an important part in treatment. These are strain of the lateral ligaments and injury to the semilunar cartilages, and it is usually the ligament or cartilage on the inner side of the knee that is damaged. Both injuries are produced by the same movement and result from the inability of the muscles to protect the joint against excessive rotary movement. This sometimes causes only a ligamentous strain, but in the following circumstances it is probably the cartilage that will be injured. With the weight on one leg, the knee slightly flexed and the foot firmly fixed on the ground (e.g. a muddy football field), the body is twisted inwards. The foot and tibia cannot move, therefore the femur rotates inwards on the head of the tibia, so that its inner border moves backwards relative to the inner border of the tibia. The internal cartilage is thus held forwards by the tibia, to which it is attached, and forced backwards by the femur until the strain becomes great enough to break it. The external cartilage is injured by the reverse movement.

The *differential diagnosis* between ligamentous strain and a cartilage injury is important because the prognosis is so different. The distinction is difficult at times, but consideration of the following points usually leads to the correct diagnosis :—(1) In cases of strain of the internal ligament the typical position for the point of maximum tenderness is at the insertion of that ligament into the tibia; this point is well below the line of the joint. The point of tenderness when the internal cartilage is injured is exactly on the line of the joint a little way internal to the patella ligament. (2) The history of the accident in cartilage injuries, particularly of the first accident if there have been several, is typical and is of the sort described under the mechanism of the production of the injury. (3) After a cartilage injury, the knee is often locked in a bent position. This may also occur when there is a "loose body" in the joint, but never following a simple ligamentous strain.

Strain of the ligaments of the knee joint must be treated energetically from the very start by massage and active movements. Elastic pressure may be applied for a few days to limit effusion into the joint, but the bandage must be removed daily to permit treatment. There is no reason to stop weight-bearing unless a ligament is severely damaged. Unless the injury is thus actively treated there is a great danger that it will develop into a state of "chronic strain." Nearly every case of chronic knee strain that one sees gives a history of an acute strain treated by prolonged rest; these patients are the bone-setters' joy, for they respond almost magically to manipulation.

Cases of injury to the *semilunar cartilages* follow one of two courses. The patient, his friends or his doctor may straighten the knee, which then never again gives trouble; or alternatively, the patient becomes the subject of recurrent attacks of cartilage trouble. The explanation usually given of the first course is that the cartilage has been "reduced," i.e. put back into its normal position, the torn surfaces uniting; whilst of the second it is said that the fragments will not unite and the cartilage "keeps on coming out." This explanation is completely fallacious. The torn bit of cartilage is not reduced to its normal position; it is dislocated usually into the middle of the joint where, with any luck, it may lie undisturbed. Subsequent trouble arises either from the dislocated or the remaining portions of the cartilage getting caught again between the bones.

It follows therefore that, when a case of injury to a semilunar cartilage is manipulated, in no sense of the word is the trouble cured. It is merely postponed and the chance that it will not recur is small. The best advice to give is manipulation after the first attack, hoping for the best, but if the trouble recurs the cartilage should be excised forthwith. If the patient is allowed to go on and on with recurring attacks until the inevitable sequel of osteo-arthritis supervenes, it is then too late to undo the damage.

THE ELBOW

There is, with a few minor exceptions, only one condition around the elbow joint which calls for manipulation, and that is the one commonly called "tennis elbow." Tennis elbow is now used as a generic term to cover any ligamentous or muscular strain occurring near the elbow, whether or no it is due to playing tennis. The pathology is identical with that of strain going on to adhesion formation anywhere else in the body. The lesion, whatever the manner of its production, is practically confined to two situations, one of which is much commoner. The common site for pain and tenderness is on the outside of the elbow joint just below the external condyle of the humerus. This spot is in the origin of the common extensor tendon and exactly over the line of the radio-humeral joint. Localization is very accurate and a tiny thickening can sometimes be felt. Pain can be produced by active or passive extension of the elbow with the wrist fully flexed and the forearm pronated. The less common site for the lesion is just internal to the upper angle of the olecranon, and pain is produced by full extension with the wrist extended and the forearm supinated.

The manipulation of tennis elbow does not give uniformly good results, relieving perhaps not more than half the cases. Sometimes when manipulation has failed, hard, deep massage will succeed; and sometimes manipulation will succeed when massage has failed. In yet other cases it may be necessary to resort to excision of the fibrous nodule which is to be found at the seat of the trouble. If the operation is performed under a local anæsthetic infiltrating only the skin and deep fascia, the patient still has sensitivity in the spot to guide the operator to it.

Manipulation should always be performed under an anæsthetic and the movements which were previously found to produce pain are carried to their extremes. It is advisable to perform the movements in all possible ways. That is to say, that when the lesion is on the outer side of the elbow, the wrist is placed in full flexion with the forearm pronated and the elbow is then sharply extended; next, with the wrist in flexion and the elbow extended, the forearm is pronated; and, finally, with the elbow extended and the forearm pronated, the wrist is flexed.

CASE REPORTS:

A SMALL PREMATURE INFANT

By J. D. HOULIHAN, B.A., M.B., B.Ch., B.A.O., L.M.
Medical Officer of Health, Birr and Killyon District, Offaly.

I SHOULD like to record a very small premature male infant, born on July 29, 1932, and weighing at birth only 1 lb. 7½ oz.; he measured 14 inches in length. The child was not expected to be born until October 22, so that he was barely a 6½ months child; it was a very difficult primipara confinement, and I was very much surprised to find that the child was born alive.

Apparently the lowest weight recorded in the literature of a child born alive is 1 lb. 5 oz., reported by Heléne Fischer-Bán in 1931[1]; this child, after very difficult rearing for four months, ultimately grew up into a perfectly normal child. John Gibbens[2] published recently an interesting article on small premature infants, recording the births of three infants at Queen Charlotte's Hospital, weighing, respectively, 2 lb. 1 oz., 2 lb. 4 oz., and 2 lb. 4 oz. He gives details of the rearing of these infants, maintaining heat with an electric pad, and emphasizing the value of precise technique in feeding; at Queen Charlotte's Hospital they are in the fortunate position of having plenty of breast milk ready to hand; as soon as the infant appeared tired during a feed, all subsequent feeds were given by an œsophageal tube for a few days.

As regards my own case, in order to think of any success in keeping the child alive I had to procure a day nurse and a night nurse to attend him all the time. I may say now that were it not for the skill and attention of these nurses the child could not possibly be alive. The clinical picture presented by the baby was one not to be easily forgotten; the body was quite limp, with scarcely any movement of the limbs, the skin was almost transparent, the respirations scarcely perceptible, with an occasional low, feeble whine.

At a loss to know where to put him in order to keep him alive as long as possible, a happy thought occurred to put him in the hot press, and as will be seen later, he was kept there continuously until the beginning of the twelfth week. This was an ordinary hot press in a fairly small bathroom. It was 4 feet long, 2 feet deep, and 7½ feet high, with four compartments separated by shelves. The baby was placed in the second from the top, the two lower compartments being mostly filled by the cylinder; the hot pipe went up through the centre of the baby's compartment, thus obviating the necessity for any extra heat in the shape of hot bottles; the door of the hot press and the bathroom window were kept open constantly.

The infant's skin was rubbed all over with olive oil twice daily, and then the entire body, including the extremities, was rolled in cotton wool; then the body was wrapped in blankets and he was placed in the hot press, where he remained for nearly three months. The temperature of the hot press was kept between 90° and 95° F.; this had, of course, to be regulated by the kitchen fire, and it is extraordinary how well it can be done after a little practice. There were two bath thermometers kept in the hot press, and the baby's temperature was taken frequently, as the body-heat was greatly influenced by the temperature of the press. On one occasion, when I took the baby's temperature, I found it 103° F., the reason being that the hot press registered 98° F.; after lowering the temperature of the hot press, the baby's temperature came down at once.

The next problem after the heat problem was nourishment; as the infant was totally unable to suck we had to use a medicine dropper. The day after the child was born we started to give him a couple of drops of water and a little sugar every quarter of an hour; the next day we gave him Nestlé's milk, about 30 drops every half-hour, and this was the diet for the first week; the Nestlé's supply was made every 24 hours, in the proportion of a small teaspoonful to 3 oz. of water; the baby also got drops of water without sugar in between the feeds. The medicine dropper had to be used for four weeks. The quantity of the food and the time between feeds was gradually increased, until at the beginning of the fourth week he was taking about six times the full medicine dropper, which held 30 drops at each feed, and the interval between the feeds was one hour. He showed sign of being able to suck at the beginning of the second week, but could not take a teat. At the beginning of the fifth week he was able to use the teat in a small bottle, and took a half-ounce of food every hour, the food being slightly increased in strength. At the beginning of the seventh week he was taking ¾ oz. slightly stronger food every 1½ hours. During the sixth and seventh week he had alternate feeds of sherry whey, which increased his weight considerably; a 24 hours' supply of sherry whey was made, 10 oz. cows' milk to 2 oz. sherry. These are the weights at the end of each week :—

At birth	- 1 lb. 7½ oz.	7th week	- 3 lb. 3 oz.
1st week	- 1 lb. 10½ oz.	8th ,,	- 3 lb. 10 oz.
2nd ,,	- 1 lb. 14 oz.	9th ,,	- 4 lb. 6½ oz.
3rd ,,	- 2 lb. —	10th ,,	- 4 lb. 14 oz.
4th ,,	- 2 lb. 3 oz.	11th ,,	- 5 lb. 5¼ oz.
5th ,,	- 2 lb. 6 oz.	12th ,,	- 5 lb. 10¼ oz.
6th ,,	- 2 lb. 12½ oz.		

At the beginning of the eleventh week he used a larger bottle.

taking 1 oz. to 1¼ oz. food every two and a-half hours, in the proportion of a level teaspoonful Nestlé's to 1 oz. water and about 8 drops of lime water in each bottle. The baby was now out of the hot press for a week and transferred to a nursery with a temperature of 68° F. He is now taking 1¼ oz. to 1½ oz. at each feed every three hours, the strength of the food being the same. After being two days in the nursery he is being dressed like an ordinary baby, the cotton wool being removed, and he is slightly smeared with olive oil at night. From the commencement the kidneys and bowels functioned normally, the bowels acting regularly twice a day.

I see no reason why this child should not now, four months later, do very well, and the lesson to be derived from the case is that many small premature children, whose expectation of living might be regarded as hopeless, can be saved by careful and constant attention after birth. This case also proves how a very small premature child can live and do well without having recourse to an incubator or, indeed, to modern hospital equipment.

References

[1] Fischer-Bán, H.: *Klin. Woch.*, 1931, x, 1354.
[2] Gibbens, J.: *Queen Charlotte's Quarterly*, October, 1932, iii, 11.

PINK DISEASE TREATED BY LARGE DOSES OF FRUIT JUICE

By HOWARD B. GLADSTONE, M.D., C.M.

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PINK disease (erythrœdema polyneuritis), an inflammation of the sensory peripheral nerve fibres resulting in cold extremities, general wasting, nasal catarrh and a rash on the hands, feet, nose, forehead and chin, has a delayed convalescence, as in the following case:—

Pamela G., aged 19 months, weight 19 lb. 5 oz., came into the Sydenham Infant Welfare Centre on November 28, 1932, from a London hospital, for convalescence. The interesting point in her case is that while for the first seven weeks she made no improvement, she began to put on weight at once rapidly and regained her health, when in place of two of her milk feeds, two feeds 5 oz. of fruit juice were given. On admission her face was covered with a rash, she could not stand, had wasted limbs and some signs of rickets. Treatment began with a little marmite, infra-red light ten minutes daily, and ultra-violet rays twice a week. Diet: Cow and Gate milk for five weeks, during which she gained 1½ lb. Then a change to fresh milk caused a loss of 2 lb in two weeks. During the last week her diet was Benger's food (20 oz. milk, 10 oz. water, 8 teaspoonfuls Benger's). At the end of seven weeks her general condition was unchanged, her motions always very offensive (two or three daily), and she had lost ½ lb. On January 17, 1933, she was given the same diet, but only three feeds of it, and two feeds of fruit juice, 5 oz. each. This 10 oz. represented the juice of four oranges and one apple. The apple is shredded and then squeezed in a meat-juice press. The daily gains in weight in the next three days were 2 oz., 8 oz., 4½ oz., and this was maintained as she put on 22 oz. in the first two weeks and 34 oz. in the following four weeks. During the first ten days only three feeds of Benger's food were given, but after that four feeds, representing 18 to 20 oz. of milk and 7 to 8 drachms of Benger's. The child was very fond of the fruit juice, took up the cup and drained it at once with great relish, but did not care for her milk meals, which had to be fed to her from a spoon at first. The general condition mended at once; in two weeks she could stand, and a week later walk. The rash on the face cleared up and the colour became good and her spirits excellent so that she played and laughed. The temperature, which had often been up to 100° F. and once to 103° F., became normal and the stools which were horribly offensive became inodorous.

In 1916 I described[1] the administration of 20 oz. of fruit juice daily to infants with beneficial results to the intestinal flora and consequent gain in weight. Since then I have found two feeds of 4 or 5 oz. are sufficient to produce the same good results. These fruit feeds are given instead of two milk feeds and not in addition to the previous food. As pink disease has usually such a long convalescence it seems worth while to record how remarkably successful fruit juice was in this case.

Reference

[1] Gladstone, H. B.: The Practitioner, 1916, xcvii, 472.

AN UNUSUAL CASE OF POISONING

By N. C. HYPHER, B.Sc., M.R.C.S., L.R.C.P.
Deputy Medical Officer, Slough Infirmary.

IT is not often that a practitioner, confronted by a case of poisoning by hypnotic drugs, can estimate the magnitude of the final dose taken by the victim. Usually the patient obtains a quantity of the hypnotic and after taking a number of regular doses according to prescription, he or she decides to finish the matter by a "grand slam." The quantity ingested at the final dose then becomes a matter for debate between the pathologist and the victim's doctor, with the coroner acting as chairman.

In the following case 24 tablets of luminal (2 grains each), were prescribed to a panel patient and the prescription given to his wife with the instruction that one tablet only was to be administered by her at 10 p.m. every night. The patient, aged 42, was a manic-depressive, who complained of melancholia and suicidal tendencies. On one occasion the man entered my surgery with abrasions around his neck and said that he had just tried to hang himself. His wife complained that she could not sleep at night because her husband walked about worrying about his work, but regarded her husband's suicidal talk as mere vapourings of the brain. She administered two tablets of luminal according to schedule on two successive nights. On the second day she went out to work and on returning home in the afternoon discovered her husband lying comatose on the bed. The box which had contained the tablets was empty; 22 tablets—44 grains—of luminal had been swallowed between 9 a.m. and 5 p.m.

I arrived at about 6 p.m. and found the man in a comatose state, with noisy stertorous breathing, slow steady pulse of good tension, pupils contracted and unresponsive to light or touch. He moved his arm, however, when a hypodermic injection was given; 1/30 gr. of strychnine and 1/15 gr. of apomorphine were given in this injection, but failed to rouse him or cause emesis. Next morning he was still unconscious but made purposeful movements when attempts were made to rouse him. The opportunity was taken to summon a Justice of the Peace to certify him for removal to the county mental hospital. In the circumstances his removal to hospital was uneventful. Enemas were administered at the institution, but at no time was a stomach tube passed. He regained consciousness on the third day after sleeping 48 hours. Two months later he was discharged from the institution fit and well.

This case is of interest in view of the varying opinions regarding the toxicity of luminal. At no time did the man appear to be in danger of death, and I did not pass a stomach tube while the opportunity presented for peaceful certification and removal. I would point out that toxicological authorities recommend gastric lavage in cases of poisoning by the barbituric group (to which luminal belongs) and I agree with this procedure, even though I did not adopt it in this particular case.

TWIN TUBAL PREGNANCY: RUPTURE

By J. A. DAVIES, L.S.A.
Medical Officer, Cottage Hospital, Towyn, Merioneth.

THE following case of twin tubal pregnancy seems to be of sufficient interest to be put on record :—

A married woman, aged 28, a primigravida, was admitted to the Cottage Hospital, Towyn, on October 10, 1932, with a history of missed menstruation for two weeks, severe occasional pain in the lower abdomen on the right side, and no vaginal discharge. On the third day after admission she had a slight vaginal hæmorrhage followed by sudden collapse, pallor, quick pulse, normal temperature, shock, with all the signs of impending death. I at once decided to operate. Under a general anæsthetic, ether, an incision, 3 inches, was made over McBurney's point, as the pain was chiefly on the right side, and the abdomen opened. After removing a large quantity of blood, it was found that the right tube had ruptured and that the ovum had escaped into the peritoneal cavity. The tube was seized and clamped both ends and removed. She made a good recovery and was up and about before the end of three weeks.

On November 3, exactly three weeks after the first operation, the patient was again seized with acute pain in the left lower abdomen, with all the previous symptoms of internal hæmorrhage and collapse. I operated at once and found that the left tube had ruptured; the ovum had escaped into the peritoneal cavity and could not be found. I did not remove the tube, but after clearing the blood out a large drainage tube was inserted; this was removed in 24 hours. The patient made a good recovery and was discharged from hospital on December 15.

PRACTICAL NOTES

PRACTICAL HINTS FROM GENERAL PRACTITIONERS

A large number of "practical hints" have been received from practitioners in response to the invitation last month (THE PRACTITIONER, April, 1933, cxxx, 510) *and a selection of these will be published in the June or July numbers. Further contributions are invited, not exceeding* 500 *words, embodying practical hints and new prescriptions useful to general practitioners.*

Exophthalmic Goitre without Increased Basal Metabolic Rate

During the first few years of the popularity of the basal metabolic test for exophthalmic goitre, the procedure was regarded as imperative in diagnosis. It was universally believed that a metabolic rate exceeding plus 10, 12 or 14 per cent. was conclusive, and despite the presence of other significant clinical symptoms, the absence of high metabolic readings was generally regarded as indicating the absence of the syndrome. However, during the past several years many clinicians have found it necessary to change their views. Here and there they discover an otherwise typical case of Graves' disease with a metabolic rate distinctly within conventional normal limits. These cases are accumulating because there is more consciousness of the prevalence of Graves' disease and more alertness in its diagnosis. Israel Braun publishes (*Endocrinology*, January–February, 1933, xvii, 23) study based upon a series of 220 cases of Graves' disease characterized by an absence of heightened basal metabolic rate and usually an absence of the customary loss in weight. His experience indicates that this type of Graves' disease may be divided into five sub-types: Untreated cases, instances of so-called "burned-out" thyroid, iodinized patients, subtotally or totally thyroidectomized patients, and patients who have undergone excessive X-ray therapy. An examination of the evidence produced by Braun indicates that symptoms of Graves' disease may persist in the absence of thyroid hyperfunction. Though possessed of little or no demonstrable thyroid tissue and rather inadequate thyroid function, yet these patients presented exophthalmos, tremor, palpitation, emotionalism, insomnia, marked fatigability and other evidences of Graves' syndrome often modified by symptoms of hypothyroidism or of myxœdema. It would therefore appear that while the thyroid is probably an almost constant participant in Graves' disease structurally, almost invariably becoming hyperplastic to some degree, demonstrable hypersecretion is not imperative in diagnosis. The presence of normal weight or overweight in a number of instances was consistent with metabolic findings. In view of these findings it would appear reasonable to infer that the tachycardia, nervous excitability, exophthalmos, and possibly all the other symptoms of

Graves' syndrome are dependent upon factors predominantly other than thyroid excitability, and that we must look to the vegetative nervous system and the other ductless glands for etiological data, thyroid participation being rather tangible in most cases, intangible in some.

Do Carcinomatous Growths secrete a Hormone?

H. O. Neumann, of the University Gynæcological Clinic in Marburg, has conducted an extensive investigation into the effect on the body of certain ovarian tumours which he calls "granulosa cell tumours." He published his first observations on these tumours in 1923, and although publication had previously been very scanty, since then several authors have recorded their findings. The peculiar construction of these tumours, which are ovarian carcinomas, enables them to be divided as follows: (1) "folliculoid" type; (2) pronounced folliculoid type; (3) mainly cylindromatous; and (4) completely cylindromatous. He established that granulosa cell growths were tumours which had a rejuvenating or a feminizing influence on the senile or infantile uterus. A few cases of these tumours in infancy have been recorded, and in association with them there has occurred premature development of sexual characteristics: genital hæmorrhage, growth of the breasts, and even galactorrhœa, growth of axillary and pubic hair, and feminizing of the whole body. All these evidences of puberty disappeared on removal of the tumour. Cases are reported of tumour at the commencement of sexual life, accompanied by menstrual disturbances which disappeared after operation. At sexual maturity, the effects of the tumours are striking. Even in women who have given birth to children, prolonged genital bleeding may suddenly occur, and may be interrupted by long periods free from hæmorrhage, up to several months duration. After removal of the tumour, regular menstruation is re-established. Towards the end of sexual maturity these clinical symptoms are less pronounced. The author states that the tumours are relatively benign, although they are unquestionably carcinomas. The occurrence of the growths at the menopause is most frequent, and the symptoms are more easily recognized. The chief feature is genital bleeding and hyperplasia of the endometrium. These findings, supported by many observers, seem to show that the tumours produce a definite hormone.—(*Endokrinologie*, March, 1933, xii, 166.)

The Effect of Diet upon Ocular Lesions

Since Bouchard, in 1886, observed that the administration of naphthalene to rabbits caused cataract, a large number of ophthalmologists have been attracted to the possibilities of this substance as a means of producing cataract experimentally. But most workers have encountered difficulties in the employment of this technique, the chief one being the remarkable variability of the effects produced by the dosing of naphthalene. Margherita Cotonio Bourne (*British Journal of Ophthalmology*, April, 1933, xvii, 210) has found that the type of ocular lesion produced in rabbits by naphthalene depends upon the diet. In animals feeding upon oats and cabbage, crystals are laid down in the retina; retinal exudates sometimes appear, but are limited in extent and never become confluent; the lens is either completely protected, or if affected, the changes do not advance beyond the stage of early peripheral striae. The protective effect is believed to be due to the cabbage. On diets of bran and carrots, or of oats, bran and carrots, extensive retinal exudates and lens changes leading to complete cataract are produced. Retinal crystals were never observed on this diet. In a few cases there was rapid death of the animal without the occurrence of any lesion except a slight swelling and haziness of the lens.

The Value of Wheat Bran, Agar-agar and other Laxatives

George R. Cowgill and Albert J. Sullivan publish a study (*Journal of the American Medical Association*, March 18, 1933, C, 1795) of the laxative values of commercial wheat bran, a processed bran product, and a mixed diet of fruits and vegetables, studied in a group of six male patients exhibiting varying degrees of constipation. The patients subsisted on carefully selected diets, the fibre contents of which were determined by chemical analysis. In all but one instance the commercial bran and the processed bran product, when fed in such amounts as to bring daily fibre intake up to 90 mg. per kilogram of body weight, were very efficacious in correcting the constipation in contrast to fruits and vegetables, which proved to be satisfactory in only two cases. The commercial bran proved to be slightly superior to the processed bran product but was much less palatable and proved difficult to ingest in reasonable quantity; no difficulty whatever was experienced in eating the processed product. It is suggested that the smaller size of the fibre particle in the processed bran product is a factor tending to decrease slightly its laxative value. In the three cases in which satisfactory laxation was not secured when the patient was subsisting on the diet of fruits and vegetables, addition of the processed bran product resulted in the desired improvement. A diet of common foods that will suffice to promote satisfactory laxation in healthy persons evidently will do so in some of these patients but not in all, and, therefore, the latter require some form of roughage that will resist all decomposition. Both commercial wheat bran and the processed bran product tested in this study were found to be satisfactory sources of fibrous roughage for these patients. In the one case presenting the picture of so-called irritable colon, fibrous roughage in any form, whether commercial wheat bran, a processed bran product, or fruits and vegetables, was contraindicated. Agar-agar, on the other hand, when fed so as to give a roughage intake of about 50 mg. per kilogram daily, gave very satisfactory results; when fed at a 90 mg. level of daily intake, it could not be tolerated. This observation in a single case suggests the advisability of further study of the clinical value of agar as a source of roughage.

The Treatment of Trigeminal Neuralgia

J. Sigwald, in discussing (*Journal des Praticiens*, March 25, 1933, xlvii, 185) the various methods of treating trigeminal neuralgia, favours section of the trigeminal nerve above the Gasserian ganglion. This, however, is a serious operation which belongs to the scope of the neuro-surgeon, not the practitioner, and other methods of treatment which he mentions have frequently to be relied upon rather than such a severe procedure. Injection of alcohol into the nerve certainly relieves many cases, even when it does not cure them, and is not difficult to carry out when a careful study of the anatomy of the parts has been made. Radiotherapy has also had successful results, therapeutic X-rays being directed to the ganglion. Ionization with aconitine or with calcium chloride has also proved successful, carried out thrice weekly for a month. The following prescription may alleviate the severe pain for a time at least :—

℞ Aspirin	gram 0·4	(grs. vi)
Pyramidon	gram 0·25	(grs. iv)
Pulv. opii	gram 0·02	(gr. ⅓)

Sig. : Take in a cachet.

Injections of parathyroid extract, insulin and horse serum have all also brought about temporary alleviation.

The Value of Nembutal in Obstetrical Analgesia

L. M. Randall, of the Mayo Clinic, has published a review (*Proceedings of the Staff Meetings of the Mayo Clinic*, March 15, 1933, viii, 166) of analgesic agents used in 160 obstetrical cases, with special reference to the results obtained from the oral administration of pentobarbital sodium (nembutal). Of the patients, 113 were primigravidas and 47 multigravidas. In the past the multigravida has not been afforded analgesia because of the fear that drugs such as morphine would narcotize the infant, if delivery should occur sooner than expected. Given an analgesic agent in which this effect need not be feared, a higher percentage of multigravidas can be relieved of pain. The author in this article makes no attempt to evaluate analgesia with gas oxygen, which was given to practically all patients in the second stage, or the anæsthesia used for delivery. In 99 (61 per cent.) of the cases, nembutal was used alone, and in 142 it was used either alone or in combination with other drugs, either morphine or colonic ether or both. The author, after a careful study of the efficacy of the analgesia with nembutal, comes to the conclusion that it has been of definite value for obstetrical analgesia, and that the margin of safety appears to be great, in that no instance of deleterious effect on the mother or infant was noticed. He gives one and a half grains of nembutal by mouth (in a capsule); this dose is repeated in twenty or thirty minutes, and again, if the effect is insufficient, in thirty minutes. Variation in dosage must necessarily depend on the effect, and the patient must be carefully observed during this period. The average dose has been 4½ grains, though 6 and 7½ grains have been given. An initial dose of 3 grains may be used if the pains are frequent and severe.

R R

REVIEWS OF BOOKS

Psychology of Sex: A Manual for Students. By HAVELOCK ELLIS. London: William Heinemann (Medical Books), Ltd., 1933. Pp. xi and 322. Price 12*s*. 6*d*.

THE author, who is a medical man and a poet, is well known for his publications during nearly forty years on the subject which he now presents with the sub-heading " the biology of sex, the sexual impulse in youth, sexual deviation, the erotic symbolisms, homosexuality, marriage and the art of love." This work is not intended to be an abstract of the author's seven volumes of " studies in the psychology of sex," but as an introduction to the chief aspects of sexual psychology. This it undoubtedly is in a manner admirable alike in the style and the substance of a subject which is surrounded with difficulties. After a summary of the necessary information on endocrinology the nature of the sexual impulse is discussed, and it is pointed out how inaccurate and misleading was the old belief that it was simply the expression of a need of evacuation, comparable to that experienced periodically in the alimentary canal and the bladder; the author modifies Moll's theory with the aid of the least contested part of the Darwinian doctrine of sexual selection, namely, that it is during the slow process of " tumescence " that sexual selection is decided, and that " detumescence " is the end and climax of the whole drama; it is certainly an anatomico-physiological process, but one that inevitably touches psychology at every point. In the chapter on the sexual impulse in youth the existence of its manifestations at an earlier age than was formerly held is accepted, but Freud's conception of the Oedipus complex is criticized and the author says we may now look " back serenely on it and the ferocious reactions it seems to have evoked." In the full chapter of sixty pages on sexual deviation it is first shown that the word " perversion," which was formerly used in this sense, is completely antiquated and mischievous, for it conveys the impression of sin and moral delinquency. The account of homosexuality contains a section on transvestism or sexo-æsthetic inversion in which the subject adopts the dress, general tastes, conduct and emotional disposition of the opposite sex; this may be associated, but is not identical, with homosexuality, and the author regards as the more suitable name for it " eonism," after the Chevalier d'Eon de Beaumont, who was generally regarded as a woman. On the problem of sexual abstinence it is definitely stated that the difficulties of sexual abstinence, even though not involving any great risk to life or sanity, are still very real to many healthy and active persons. This is an authoritative work, moderate in tone, extremely well written, and fully up to date from a scientific point of view.

Inherited Abnormalities of the Skin and its Appendages. By E. A. COCKAYNE, D.M., F.R.C.P. London: Humphrey Milford (Oxford Medical Publications), 1933. Pp. x and 394. Plates 2, numerous pedigrees. Price 32*s*.

THIS is a new departure, for no previous attempt has been made to deal with the genetics of all the defects of any one part of the body in a single volume. Dr. Cockayne, who has done much valuable work on the Mendelian aspects of disease, has now brought together in a wonderfully complete and scholarly manner the abnormalities which cause changes in the skin, teeth, hair and nails. This veritable treasury of information, largely about rare conditions, is the outcome of an amazing amount of research and of much personal observation, which obviously must have extended over many years. After an introductory chapter on Mendelian heredity physiological abnormalities, such as piebalds, are considered, and here, as elsewhere, many interesting examples are unearthed. Under the heading errors of development of elastic tissue hereditary telangiectasis, cutis hyperelastica and epidermolysis bullosa are described, and in the accounts of the first attention is drawn to its occurrence in famous racehorses, such as Herod (1748), Hermit, Gallinule and Humorist. In the section on dyskeratoses the subject of ichthyosis is remarkable, even in this monumental work, for its wealth of detail. A specially interesting section deals with ectodermal dystrophies; thus the " cagots," who live in the south-east of France, near the Pyrenees, have been regarded as cretins or lepers, but are shown to be the subjects of hypotrichosis et dystrophia ungum. The curious condition of hypertrichosis lanuginosa (dog-faced type), characterized by persistence and excessive growth of the lanugo hair in all parts of the skin, and giving the victims a grotesque appearance like that of a skye terrier, is illustrated by the frontispiece. Among the disorders of growth the subject of neurofibromatosis or von Recklinghausen's disease is exhaustively treated and special attention is paid to the hereditary aspect. This must long remain a much consulted book of reference, more particularly by dermatologists.

Nervous Diseases in Infancy and Childhood. By NEILL HOBHOUSE, M.D., M.R.C.P. London : H. K. Lewis and Co., 1932. Pp. viii and 212. Figs. 4. Price 8*s*. 6*d*.

THIS does not profess to be a textbook, but it is a series of clinical studies from a practical point of view beginning with birth injuries and ending with psycho-neuroses and mental deficiency. Under disorders resulting in cranial abnormality, the author places hypertelorism, in which the essential defect is a disproportionate development of the sphenoid bone, the lesser wing of which is unduly large; it is sometimes described among the mental deficiencies, but his experience leads him to regard this as not a constant association. From his own observations he comes to the conclusion that syphilis plays a remarkably small part in the causation of nervous disorders in childhood, and that the incidence of syphilitic manifestations in the nervous systems has been overestimated on the basis of positive blood Wassermann reactions without this test of the cerebro-spinal fluid. The myopathies, though without any nosological connection, are described with the abiotrophies Friedreich's disease and hereditary cerebellar ataxia, as they present the same slowly progressive, crippling and similar problems in their treatment and management. In the chapter on some disorders of the peripheral and autonomic nerves, achalazia of the cardiac orifice of the stomach, pink disease, angio-neurotic œdema, Raynaud's disease, and amyotonia congenita are included. There is a good account under the heading of hyperkinesis of the forms of abnormal movement, including what the parents commonly call "fidgetiness," a very practical subject.

A Shorter Orthopædic Surgery. By R. BROOKE, M.S., F.R.C.S. Bristol: John Wright and Sons, Ltd., 1932. Pp. 144. Illustrations 126. Price 10*s*. 6*d*.

THIS small book is stated by the author to be devoted essentially to the instruction of house surgeons and masseuses, yet it contains exhaustive detail in compact form. The descriptions of the various pathological states are generally lucid, though some points could be presented with further clarity. The classifications of the different diseases do not conform to the standard of the book in general, and some time-honoured and fundamental points could be included with advantage, among these may be mentioned the frequency with which patients with hip disease present themselves because of symptoms referable to the knee, also the value of Shenton's line in the description of radiographs of the hip. It is difficult to believe that dancer's feet are usually of the "cavus" type, and that the "carrying angle" is greater in the male, in view of the increased width of the female pelvis. The occurrence of incontinence as a sign of implication of the cord in Pott's disease is surely late in onset and one indicating extensive involvement of the cord; further the induction of pressure on the cord in spondylolisthesis cannot well be a common accident, as the cord ends at a higher level. The small amount of flexion advised for cases necessitating fixation of the hip will not meet with generalized acceptance. The illustrations are excellent, well chosen and well reproduced, consequently of much practical value.

Minor Ailments and their Treatment. By LEONARD WILLIAMS, M.D. Sixth edition. London: Baillière, Tindall and Cox, 1933. Pp. xiii and 420. Price 11*s*.

As this is the sixth edition of a work which first appeared in 1906, there is not any need to point out that it meets a popular demand, and that its success is not solely due to its matter, but to its combination with manner and wisely expressed advice. Like a laughing philosopher, the author has the happy faculty of impressing with a telling phrase the points he makes as the outcome of experience and shrewd observation. While retaining the fascination of style the volume keeps pace with modern fashion, and as "goutiness" is no longer "in the movement," the chapter formerly so entitled is now headed "salient symptoms," and deals with some of the most prominent features of the gouty diathesis in such a manner as suggest their relation to other conditions. Boils sometimes ascribed to poor blood are rather the outcome of plethora, and some of the common methods of treatment meet with such outspoken criticism that probably few who read his graphic condemnation of squeezing them will continue to do so with a heavy hand and a light conscience. Another section, that on insomnia, in this chapter is packed with useful hints as regards the detection of the causal factor and its successful treatment. The chapter on the forms of dyspepsia, other than those sometimes called surgical, namely, those due to ulcer, growth, appendicular and gall-bladder irritation, has been revised with similar success.

Hints to the Young Practitioner. By G. FRANCIS SMITH, M.R.C.S., L.R.C.P. Oxford University Press; London: Humphrey Milford, 1932. Pp. vii and 150. Price 5s.

MEDICINE is in its different aspects both a science and an art; the science is taught in the much overburdened curriculum which probably most teachers feel should be curtailed in directions other than their own. But much of the art of private practice, how to manage patients and their friends is not taught in medical schools, as the recently qualified man soon finds out when he starts in general practice. Some years ago the late Sir James Mackenzie, who was in general practice at Burnley for 28 years before he became a consultant in London, fully recognized this want in medical education and, to remedy it, advocated that every medical school should have among its teachers at least one with ten to twenty years' experience of general practice. As a substitute for the guidance which would have been provided had this advice been acted upon, the newly qualified man may with advantage turn to the sound wisdom which, with the experience of 46 years in general practice, during more than thirty of which he was a police surgeon, Dr. G. Francis Smith dispenses in a pleasantly written book with plenty of short stories, some against himself, to point the moral. Few men realize when they start what general practice means, and one of the first things to remember is the care that should be taken before entering into a partnership. The difficulties are so explained that the reader is comforted rather than dismayed at the prospect. That the life is strenuous is frankly faced, but Dr. Smith provides a philosophy, even for night calls. In the days now almost forgotten when the apprenticeship system was in vogue there was not the same need for instruction in the art of general practice as now exists, and the remedy which the author proposes, though it is hardly likely to become available, is that there should be a shorter curriculum for examination, and that the time thus saved should be given up to a six months post-graduate course before the newly-qualified man be allowed to register and practise.

Clinical Ophthalmology for House Surgeons and Students. By J. MYLES BICKERTON, M.A., B.Ch., F.R.C.S., and L. H. SAVIN, M.D., M.R.C.P., F.R.C.S. London: H. K. Lewis & Co., Ltd., 1933. Pp. 147. Illustrations 92 (including 6 plates). Price 7s. 6d.

THIS book is intended for house surgeons and students, and contains chapters on methods of clinical examination, diseases of the lids and orbit, " forms " of conjunctivitis, " some affections " of the iris, ciliary body and sclera, corneal diseases, diseases of the lacrymal apparatus, cataract, glaucoma, sight-testing for beginners, squint, ocular injuries, and ophthalmoscopic appearances in disease. A chapter is devoted to the formulæ of lotions, drops, ointments and other therapeutic agents of pharmacological importance, and there is an appendix of instruments required for the standard ophthalmic operations. The use of a 2 mm. trephine is advised in operations for glaucoma and no mention is made of the 1·5 mm. trephine with which the majority of surgeons operate. It seems a pity that in those chapters which describe certain ophthalmic operations no account is given of post-operative care, complications and treatment.

The Diabetic Life: Its Control by Diet and Insulin. By R. D. LAWRENCE, M.A., M.D., F.R.C.P. Seventh edition. London: J. and A. Churchill, 1933. Pp. 218. Illustrations 10. Price 8*s*. 6*d*.

THE fact that this is the seventh edition of a book which was first published in 1925 is evidence of its popularity and usefulness. The book is intended as a dietetic guide both for the doctor and for the patient, and its reputation is now so well established that detailed comment would be superfluous. The chief alteration in this edition is the adoption of the modern practice of an increased carbohydrate intake which has so much added to the comfort and well-being of the diabetic patient.

SHORTER NOTICES

British Spas and Seaside Resorts.—Official Handbook of the British Health Resorts Association, 1933. London: 199, Piccadilly, W.1. Pp. 196. Price 1s.—This handbook is based on the well-known section by Dr. Fortescue Fox in the *Medical Directory* and is intended for the use of practitioners in choosing the places at which their patients are most likely to get the kind of climate, baths, and other treatment they may require.

The Medical Press and Circular, April 5, 1933. With Supplement on Skin Diseases in General Practice. London: Baillière, Tindall and Cox.—This is the second of the quarterly supplements published by this old-established journal and contains six practical articles on common skin diseases edited by Dr. M. Sydney Thomson.

Institute of Ray Therapy, Third Annual Report, 1932. London: Camden Road, N.W. Pp. 22.—This Institute has now been open for two years and ten months, and since January of this year 1,616 new patients have been seen, a considerable increase. We note that every new patient has to bring a letter from his or her qualified medical practitioner. This flourishing institution owes much to the energy of its honorary medical director, Dr. William Beaumont.

NOTES AND PREPARATIONS

LIVRON

Livron is a compound liver extract and iron preparation, made by Messrs. Boots Pure Drug Co. (Station Street, Nottingham). It contains liver extract (each fluid ounce of the preparation contains the equivalent of 2 ounces of fresh liver), yeast extract, ferr. et ammon. citr., ferr. et mang. citr., ext. medullae rub., glycyrrh. ammon., acid. salicyl. (2 grains in each fluid ounce), glycerin, tint. cardam. co., in liquid extract of malt. Such a preparation can obviously be criticized as being rather of the " blunderbuss " type, and one would imagine that a simpler preparation of liver extract and the scale preparations of iron might have had all the clinical usefulness of this rather elaborate one. We are assured, however, that livron has been tested and found to be clinically active and it should therefore be given a thorough trial in practice.

ADEXOLIN EMULSION

Adexolin emulsion is a new preparation made by Glaxo Laboratories (56, Osnaburgh Street, London, N.W.1), which contains vitamins A and D standardized to be equivalent to its own volume of cod-liver oil and also 7½ grains of calcium lactate in each fluid ounce. Up till now it has apparently been impossible to produce a palatable emulsion containing vitamins A and D on account of technical difficulties, but this new preparation is certainly very palatable and should prove useful in practice. The emulsion is particularly recommended for convalescents who are unable to take the usual cod-liver oil emulsion.

CARBOKAYLENE

Carbokaylene is a new preparation, manufactured by Messrs. Kaylene, Ltd. (Waterloo Road, London, N.W.2) and is composed of kaylene and highly activated vegetable charcoal. It combines the detoxicating action of kaylene, the value of which is by now well recognized in medical practice, with the flatulence-reducing properties of charcoal. It seems to us an excellent combination: kaylene is an adsorbent for bacterial toxins, toxalbumins and toxic or sensitizing proteoses, while charcoal acts as an adsorbent for simpler substances, such as alkaloids, putrefactive amines, organic acids, toxic alcohols, and gases. The preparation is indicated particularly in cases of dyspepsia, hyperchlorhydria and intestinal fermentation.

COLONATOR

The colonator is a new appliance for colonization, which makes this procedure simple and cleanly for the practitioner or nurse in charge of a case. The apparatus consists of a stout india-rubber bag, which is shaped to fit comfortably on an ordinary lavatory seat; to this is attached a rubber tube with a detachable vulcanite nozzle (in two sizes, for children and adults); the nozzle has pinhole perforations at the sides, and the volume of the flow can be increased, diminished, or cut off at once by means of a control tap. This apparatus seems to us to be very simple and convenient for carrying out colonic lavage for purposes of diagnosis or treatment. It is put up complete in a portable case of the attaché type, and can be obtained from the Colonator Co., 197 Bath Street, Glasgow, C.2.

LINGFORD'S LIVER SALT

This "liver salt" is a white powder which effervesces and dissolves at once on the addition of water and has a pleasant, clean taste. On analysis we have obtained the following result:—

Anhydrous magnesium sulphate	11·1 per cent.
Anhydrous sodium bicarbonate	22·3 ,,
Tartaric acid	22·1 ,,
Cane sugar	40·0 ,,
Moisture	4·5 ,,

It is therefore a mildly aperient preparation, the fairly large proportion of sugar masking the unpleasant taste of the magnesium sulphate, and can be used freely without any harmful results. It is packed in patent air-tight tins. The manufacturers are Messrs. Joseph Lingford and Son, Bishop Auckland.

BOURNVILLE

On a recent visit to Bournville, the "garden factory" of Messrs. Cadbury, the cocoa and chocolate manufacturers, our representative was particularly impressed with the laboratories, which are divided into a maintenance section, a developments section, a biochemical section and a research section; the laboratories also possess an extensive technical reference library. The laboratory staff numbers 35, 16 of them fully qualified chemists, under the direction of Mr. A. W. Knapp. No visitor to Bournville can help noticing the healthy atmosphere in which the employees work; for the younger employees physical training is compulsory as a condition of employment, and the boys and girls working at Bournville attend the day continuation school for one complete day each week instead of going to work. The recreation grounds extend to over 110 acres. This model factory, in pleasant surroundings, is a proof that industry need not necessarily be drab or sordid.

MESSRS. E. & S. LIVINGSTONE'S CATALOGUE

We have received Messrs. E. & S. Livingstone's (16 and 17 Teviot Place, Edinburgh) new catalogue of medical, dental, nursing and scientific books. It is produced with the same care in clearness of type and illustration that distinguishes the books published by this old-established firm, whose founders were immortalized by Robert Louis Stevenson in "Memories and Portraits"—"a pair of little active brothers, Livingstone by name, great skippers on the foot, great rubbers of the hands, who kept a book-shop over against the University building."

THE PRACTITIONER

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PULMONARY COMPLICATIONS FOLLOWING OPERATION ON THE STOMACH AND DUODENUM

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IT has long been known that operations in the upper part of the abdomen are associated with greater danger of post-operative pulmonary complications than are operations elsewhere in the abdomen. In a careful study of various abdominal operations performed in The Mayo Clinic this fact is confirmed, and it is shown that the incidence of these complications for operations in the lower part of the abdomen is approximately half of what it is for those in the upper part. Although this liability to pulmonary complications is definite, it will not contra-indicate operation in cases in which operation is otherwise clearly indicated. When the optimal time is chosen for operation, and every precaution is taken to prevent pulmonary complications, their seriousness is reduced to a minimum. As an example of this fact, Moynihan reported 1,000 consecutive operations for duodenal ulcer with one death. At The Mayo Clinic, the mortality rate for the most conservative type of operation for duodenal ulcer, namely, excision and reconstruction of the pyloric outlet, is less than 1 per cent. Data on mortality in The Mayo Clinic for the most serious gastric lesion, gastric carcinoma, show that for subtotal and total gastrectomy the hospital death-rate averaged 10 per cent., and in one consecutive series of 200 such cases reported, there were ten (5 per cent.) post-operative deaths in hospital. In another series of cases reported by one of us (Balfour) of 400 consecutive operations on the stomach and duodenum, including 113 operations for gastric carcinoma, there were four deaths in hospital. When it is considered that these mortality rates include deaths from all causes, the menace of pulmonary complications at least so far as their being directly responsible for a fatal outcome obviously is not great. At the same time, the significance of post-operative pulmonary complications following any abdominal operation, and particularly after operations in the upper part of the abdomen, should not be underestimated and, since a satisfactory explanation has not, as yet, been given for the increased liability known to be associated with operations in the upper part of the abdomen, a consideration of the possible factors and of the methods of prevention would seem to be appropriate.

Many observers have expressed the opinion that the majority of pulmonary complications are due to emboli carried from the field of operation. The result is pulmonary infarction. This usually manifests itself by rapid onset, elevation of pulse, respiration and temperature, pain and occasionally blood-tinged sputum. It is difficult to accept this explanation from an anatomical standpoint, since infected emboli cannot reach the lung through any direct venous communication. The venous drainage from both the stomach and duodenum is into the portal circulation and must pass through the capillaries of the liver before reaching the lung. If infected emboli are liberated from the operative site in surgical procedures on the stomach and duodenum frequent infectious processes of the liver might be expected to occur, but in our experience they are exceedingly rare.

The most widely accepted theory relative to the production of post-operative pulmonary complications is that which attributes the condition to the aspiration of infected material either during or immediately after the operation. With the introduction of anæsthesia by inhalation, it was felt that there was of necessity a varying degree of irritation of the lungs which created a favourable medium in which an infectious process might thrive. So far as gastric and duodenal surgery is concerned, this explanation seems plausible, since in certain operations much manipulation of the stomach is necessary, and this might give rise to reflux of gastric content and with inhibition of the cough reflex, some of the gastric material might find its way down the trachea and lodge in the lung. The chief argument against this theory is that pulmonary complications occur after spinal or local anæsthesia in which the cough reflex is not abolished. Since we have found that spinal anæsthesia is not as satisfactory as other methods of anæsthesia for surgical procedures on the stomach and duodenum, spinal anæsthesia has been used in so few cases that it is not possible to make statistical comparison, so far as pulmonary complications are concerned. The combined use of sedatives with spinal anæsthesia has become widespread. Not infrequently the patient has received so large a dose of one of the hypnotics available that he is practically asleep when he enters the operating room, and, with the opiates he receives after the operation, it is not inconceivable that even with the use of spinal anæsthesia gastric material might be aspirated. Spinal anæsthesia often causes severe nausea with vomiting. Unfortunately, this is most likely to occur when there is the slightest traction on the stomach or other viscera, and not infrequently it is necessary to combine the spinal anæsthesia with some form of anæsthesia by inhalation in order to obtain the necessary relaxation. Unquestionably the type of anæsthesia by inhalation plays an important part in this connection. Theoretically, intratracheal anæsthesia is most suitable for surgery of the stomach and duodenum if the services of one who is skilled in the use of the intratracheal catheter are available. By use of the intratracheal catheter, clear air passages are assured, and quiet, effortless respiration is obtained for a reasonable length of time. Rarely is material aspirated, because the tube is chosen to fit the trachea snugly.

Evidence in favour of the hypothesis that aspiration of material is a common cause of post-operative pulmonary complications has been contributed by those who have made use of the pharyngoscope when tracheal intubation has been attended by unusual difficulty. Often an accumulation of mucus has been observed in the posterior part of the pharynx. With each inspiration the mass is drawn toward the trachea and undoubtedly must often be aspirated. Because of the fact that the pneumococcus type IV has long been known to be an inhabitant of the oral cavity, the significance of this observation is apparent. If emboli or aspirated infected material were the explanation of post-operative pulmonary complications, the complications would occur as commonly after pelvic as after upper abdominal operations. Moreover, proximity to the diaphragm, and therefore to the lungs, of upper abdominal operations will not account for the difference.

The possibility of infection being carried through the lymphatic channels has received slight attention in the consideration of post-operative pulmonary complications. The lymphatic structures of the stomach and duodenum, as described in standard text-books of anatomy, include three groups of lymph nodes which correspond to the branches of the cœliac axis. Included in the gastric nodes are two chains which are situated respectively along the lesser and the greater curvatures of the stomach, and which are intimately associated with the greater vessels in these situations. Lymphatic drainage from the stomach and first portion of the duodenum passes to the cœliac nodes. The afferent channels of the hepatic nodes come from the liver, the head of the pancreas, and the first and second portions of the duodenum, and their efferent channels pass to the cœliac nodes. The pancreatico-splenic nodes drain those organs supplied by the splenic artery: namely, the stomach, pancreas, and spleen. The efferent channels pass to the cœliac nodes. The latter are situated in front of the abdominal aorta, near the origin of the superior mesenteric artery and the cœliac axis, and their efferent channels pass to the higher nodes of the group, and thence either directly into the receptaculum chyli, or they may unite to form a common trunk, the truncus intestinalis, which joins the left lumbar trunk to form one of the tributaries of the thoracic duct.

In the light of recent excellent experimental work on lymphatic drainage of the abdomen, the suggestion has been made that a more direct path of communication exists than that just described. Higgins and Graham, in 1928, studied the anatomical relations of the lymphatic channels which function in removal of particulate matter from the peritoneal cavity of the dog. It was found that the thoracic duct played a relatively insignificant part in this process. In normal, healthy dogs, particulate graphite, when injected directly into the peritoneal cavity, was readily visible in the diaphragmatic lymphatic structures and in the sternal trunk, within from ten to twelve minutes. The main collecting trunks of the diaphragm lay below the pleura, on the muscle bundles, and pursued in general a diagonal course from the crura to the pars sternalis. These larger channels formed a rather prominent plexus as they continued toward the sternum, and the smaller lymphatic vessels pursued parallel courses and emptied into the major plexus. Five routes of drainage were observed, by means of which the absorbed material was removed from the diaphragm. The first of these was the sternal route, by far the most effective, for it received the drainage from the pars sternalis, from the pars costalis, and to a certain extent from the pars lumbalis. The remaining four routes were found to be of about equal size and distribution. One of the four routes consisted of a group of small lymphatic capillaries which arose partly in the pars sternalis just ventral to the central tendon and partly from the muscular portion dorsal to the tendon. This group on leaving the diaphragm, coursed forward along the pericardium, often parallel with the œsophagus and the vagus nerves, to the bronchial lymph nodes which lie dorsal to the base of the lung. Another route, effecting drainage of the lymph anteriorly from the diaphragm, was found to be by way of the thoracic duct. The other two routes led directly into the peritoneal cavity or into retroperitoneal spaces dorsal to the two diaphragmatic crura. Thus the five routes through which particulate matter was removed from the peritoneal cavity of dogs were the sternal, the pulmonary, the retroperitoneal, the direct peritoneal and the route by way of the thoracic duct. Although direct pulmonary contact with peritoneal drainage was not effected, the investigators were of the opinion that by any disturbance in the flow of lymph coming from the peritoneum so as to produce stasis or even retrograde flow, the lung might be infected with organisms from the peritoneum.

Similar experiments by Lemon and Higgins confirmed the observations made by Higgins and Graham that five main channels carry the particulate matter from the peritoneum, upward through the thorax and into the blood-stream. Lemon and Higgins also were able to demonstrate the presence of a thoracic vessel which passed downward over the posterior wall of the thorax, sometimes receiving tributaries from the vessels of the posterior portion of the diaphragm, and communicating with the lymph nodes in the region of the kidney. There seemed to be no question but that normal muscular contraction of the diaphragm contributed much to the passage of particulate matter through the diaphragm. The lymphatic structures on the right side of the diaphragm were much larger, and they carried a much greater proportion of the flow of lymph than those on the left.

If the lymphatic mode of infection is accepted as being at least partially responsible for the high incidence of post-operative pulmonary complications, several controversial points may be answered satisfactorily. As has been shown, the rate at which particulate matter traverses the lymph channels of the diaphragm is greatly retarded by decreased activity of the diaphragmatic musculature. Operations in the upper part of the abdomen are attended almost invariably by a decrease in the activity of the diaphragm, and as a result two factors are brought into play which predispose to pulmonary complications, namely, decreased vital capacity, and sluggish flow in the diaphragmatic lymphatic system. It is not inconceivable that primary involvement of the pleura of the diaphragm may be the result of stasis of infectious material in the lymph spaces of this region, and that extension to the parenchyma of the lung is a secondary process.

In the experience of most observers, the right side has been the site of pulmonary complications much more frequently than the left. Lemon and Higgins found that even after the right side of the diaphragm was paralysed, the pattern of particulate matter discovered after the lapse of thirty minutes was more distinct on the paralysed right side than on the normal left side. Absorption through the left half of the diaphragm, when that half was paralysed, was insignificant. The predominance of complications on the right cannot be explained by the hypothesis of embolism. Added evidence to substantiate the hypothesis of aspiration is found in the fact that the right bronchus is a more direct continuation of the trachea than the left, and hence aspirated material is more likely to lodge on that side.

MEASURES SUGGESTED TO DECREASE THE INCIDENCE OF POST-OPERATIVE PULMONARY COMPLICATIONS

It must be admitted that no single factor is responsible for pulmonary complications following operation on the stomach and duodenum. With due consideration of the most plausible factors, both direct and indirect, the following suggestions are made in the hope that decrease in the incidence of this distressing condition may be effected. Many factors have been emphasized repeatedly by those interested in this subject, but often it is with the repetition of such well-known factors that they become drilled into consciousness. Perfectly obvious suggestions are disregarded with surprising frequency in many institutions where great pride is taken in adherence to detail.

Pre-operative prophylaxis.—Perhaps the most important factor is to ascertain the possibility of respiratory infection, however insignificant it may appear to be. If such an infection is present, operation should be postponed. Unfortunately operation is often put off for one day only after the subsidence of acute or subacute respiratory infections. At least a week should intervene between the subsidence of such a condition and any contemplated operative procedure within the abdomen, and particularly is this important for lesions of the stomach and duodenum.

Infectious processes of whatever nature should be eradicated if this is feasible, and the patient's general condition brought to its best possible state. It is only in this way that what has been so loosely termed the patient's " resistance " may be increased. Elimination, both of fæces and urine, should also be studied. The waste products of protein metabolism are retained when pyloric obstruction is present. For this reason adequate intake of fluid is essential, and frequent gastric lavage over a prolonged period may be necessary before the chemical constituents of the blood are brought within normal limits. In those cases in which pyloric obstruction is present clinically, or is evidenced by retained gastric material, the gastric contents should be thoroughly aspirated before any surgical procedure is attempted. Atropine in appropriate doses should be administered immediately before operation in order that there may be a decrease in the secretion within the oral cavity and bronchial tree to compensate for the stimulating effect of anæsthesia by inhalation.

Operative prophylaxis.—The operating room should be kept warm. What may seem comfortable to the surgeon may be too cool for a patient whose body is moist and whose capillaries are dilated. The minimal temperature of the operating room should be 78° F., and the temperature should be maintained at or slightly above this level.

The choice of anæsthesia is most important. As has been said, we have not found spinal anæsthesia to be entirely satisfactory for operations on the stomach and duodenum. The use of intravenous and rectal anæsthesia has been restricted to a small group of selected cases also, chiefly because of the difficulty of controlling the effect of the drug after it has been injected. In our hands anæsthesia by inhalation, preferably nitrous oxide or ethylene with oxygen, and ether, has been used almost as a routine, and in many instances this has been administered by the intratracheal method as recommended by Magill of London. This method is particularly valuable when the patient is of the short-necked, broad-chested type, and might reasonably be expected to resist anæsthesia. Aspiration of infectious material is less likely to occur than when intratracheal intubation has not been done, and quieter and more easily controlled anæsthesia can be effected. Ether should be used only sparingly. It is often surprising how little ether is necessary for gastric and duodenal operations, if surgeon and anæsthetist co-operate.

Extensive resection for inflammatory lesions which have developed at the site of a previously made anastomosis may be carried out with as little as 3 ounces (90 c.cm.) of ether if combined properly with either gas mentioned previously and oxygen. At the conclusion of the operation, hyper-ventilation by means of a mixture of 95 per cent. oxygen and 5 per cent. carbon dioxide may be carried out. This may be started before closure of the abdominal incision is complete, and by the time the dressing is in place and the patient ready to be moved, ample oxygenation should be in effect.

Speed, without the sacrifice of accuracy, and gentleness are two surgical attributes of inestimable value. It is obvious that pulmonary complications will occur in direct proportion to the length of anæsthesia. The type of operation should be determined with this factor in mind. Undue manipulation should be avoided, for the chance of reflux is thus increased, and, theoretically, passage of infectious material into the efferent lymphatics may result.

A suction apparatus introduced early in the course of the operation through the gastric wall quickly and completely empties the stomach and is of great value. As a result of the aspiration more satisfactory exposure often is obtained, with consequent decrease in manipulation, and the possibility of reflux is lessened. The suggestion has been made that a small tube be passed through the œsophagus and allowed to remain in place throughout all operations on the stomach and duodenum and for twenty-four to forty-eight hours post-operatively. Points in favour of this suggestion are that the stomach is kept empty at all times, the likelihood of material being aspirated into the lung is decreased, and gastric dilatation by retained material is practically eliminated. The exact situation of the tip of the tube can be determined at the time of the operation, and anxiety as to injury by the tube at the operative site is thus forestalled. There should be no objection on the part of the patient if a small nasal tube is used and held snugly in place by adhesive tape. Frequent aspiration may be accomplished without discomfort to the patient, or constant suction may be instituted with the use of a water-flow suction pump. Indwelling stomach tubes have not been used as a routine, but they offer interesting possibilities in the reduction of post-operative pulmonary complications.

The method of application of adhesive straps to the surgical dressing has not received due consideration. In a course of experiments designed to determine the factors influencing the mechanics of respiration, Lemon noted that when bandages were applied over the abdomen and the lower part of the thoracic wall, as high as the level of the ensiform cartilage, respiration was markedly embarrassed. The upper part of the thorax seemed to maintain normal movements, but

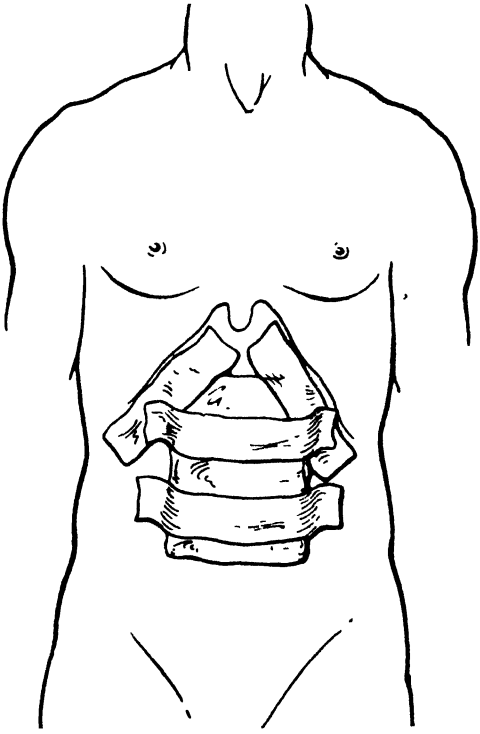

Fig. 1.—Method of applying adhesive straps to the surgical dressing.

the amplitude of the lower part could be reduced remarkably by increasing the tightness of the bandage. When the bandages were removed, the amplitude of movement promptly returned to normal, and the visible effort to maintain respiration disappeared. The fundamental principles of this observation have been utilized in the use of adhesive tape as illustrated in Fig. 1. Constriction of the costal arch is thus eliminated, and unhampered thoracic respiration effected. This factor is of particular importance to women, for the respiratory act of women is predominantly thoracic.

The position of the patient on the table has been the subject of considerable comment. In order to decrease the possibility of aspirating infectious material, a slight Trendelenburg position may be employed. Material accumulated in the naso-pharynx may be removed at intervals. This factor may account for part of the difference in incidence of pulmonary complications following pelvic operations as compared with similar complications following operations on the upper portion of the abdomen, for the former are executed with the patient in the deep Trendelenburg position.

Post-operative prophylaxis.—At the conclusion of the operation it is of the utmost importance that extreme caution be exercised in transferring the patient from operating room to bed. The patient's capillaries are dilated and the skin is moist. Thoughtless exposure of the body when dressings are put in place, and when the sterile linen is removed, may be a factor in the development of pulmonary complications. Rubbing the thorax with alcohol that has been slightly warmed, and immediate application of heated blankets, will decrease the loss of heat that undoubtedly contributes to the complications. The blankets should be kept carefully in place until the patient is returned to bed, for it seems impossible to eliminate the draughts that are invariably present in corridors of hospitals.

The patient should be placed in the modified Fowler position after the return of consciousness. In this way respiration is least embarrassed, and there is less likelihood of aspirating material into the trachea. Care should be taken to prevent the patient from sinking down while in this position, for then respiration will be interfered with, and greater harm than good will result from the position.

The immediate post-operative use of oxygen has produced inconclusive results in the prevention of post-operative pulmonary complications. If definite anoxæmia is evidenced by cyanosis, the use of oxygen should be instituted, but in ordinary circumstances an adequate supply of fresh air is ample to supply the needs. Thus the stimulus to the respiratory centre has not been removed as when oxygen alone is used, and the added expense and difficulty of caring for the patient are eliminated.

The use of carbon dioxide to stimulate respiration is based on sound theory and has been found to be extremely useful in many instances as a prophylactic measure. A mixture of 10 per cent. carbon dioxide and 90 per cent. oxygen may be given for from one to two minutes every hour for the first six or eight hours immediately following operation if indicated.

SUMMARY AND CONCLUSIONS

A general consideration of the various etiological factors in the production of pulmonary complications following operations on the stomach and duodenum has been presented in the hope that a way may be found to reduce their incidence. We feel that no single factor is directly responsible, but that individual instances may result from one circumstance or a combination of circumstances. Suggestions of practical interest in pre-operative, operative, and post-operative prophylaxis have been reviewed in order to stress the importance of adherence to detail. We feel that pulmonary complications result not infrequently because simple and obvious details have been neglected.

THE PROGNOSIS AND TREATMENT OF RHEUMATIC HEART DISEASE IN CHILDHOOD

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THE prognosis of rheumatic heart disease in childhood may be considered in the light of an investigation by the writer into the conditions found at necropsy in 100 fatal cases under twelve years of age, in 86 of which there was definite evidence of active rheumatism. This is a clear warning that the outlook of a case which at first appears to be favourable may, in the course of a few years, be entirely altered in character by renewed activity of the disease. I have not any figures for guidance in adults, but believe that a considerable advance in the knowledge of rheumatic heart disease would result from an inquiry into the ultimate failure of the heart in the rheumatic from the standpoint of renewed activity of the infection. The more prolonged supervision of children with rheumatic heart disease now being carried out in England and America should after some years give further useful and valuable data bearing upon prognosis, which were formerly not available, and is a matter of vital importance. The outlook is made more difficult because there appears at present to be no specific treatment capable of controlling the recurrence of active carditis.

There is the immediate outlook, and the distant one dependent upon the disturbed cardiac mechanism due to scarred valves. This latter question belongs to the prognosis of chronic heart disease which is beyond the scope of this article. The mortality from acute rheumatism would appear to be higher in male than female children. Of 68 males 12 died, of 104 females 10 died, but the greater frequency of the disease in females must be taken into account in a wide survey. The mortality varies in different years. Thus in 1920, when the disease was severe, out of 172 cases 22 died and 30 became complete invalids.

Great attention should be directed to the damage done to the myocardium as shown by severe dilatation and such prominent signs of toxicity as profound anæmia and continued rapidity and feebleness of the pulse. In all cases of general carditis it is the myocarditis rather than the pericarditis or endocarditis that wrecks the heart. A strong child may make a remarkable recovery from pericarditis, but a fragile child with severe myocarditis is in great danger both immediately and in the near future. It is to be remembered that there may be no fever or very little fever indeed in the most virulent carditis. Pericarditis is necessarily a serious event, in spite of the good recoveries that may occur, because it is associated with severe infection of the heart, and may leave for the future the additional burden of a pericardium adherent to such contiguous structures as the chest wall and lungs.

The mortality would appear to be greater when the carditis occurs before the age of five years. Eight cases out of 52 under my observation proved fatal, but more inquiry is still needed into the incidence and fatality of the disease under five years, which is not so unusual as generally believed. Reviewing the fatal cases of carditis in childhood it would appear that about 30 per cent. of them occur in what appears to be the first attack. When confronted with a severe case ill-omened symptoms are: increasing pulse and respiration rates, livid pallor, restlessness and vomiting. Cheadle's dictum of the serious import of subcutaneous nodules holds good in spite of the well-known exceptions that may be met with. In a recent analysis of 72 fatal cases 27 showed these nodules.

When very ill these children are strangely silent and do not waste their breath by speaking to doctors or even nurses. Death may be sudden after taking some food or in the early morning. Some make a partial recovery, but then have a slight relapse and die, or die unexpectedly from myocardial failure when thought to be improving. Anginal attacks may occur but are not frequent.

Favourable signs are when the cardiac impulse becomes palpable and circumscribed, when the deep cardiac dullness diminishes, and the child commences to take interest in its surroundings. With these there will be a fall in the pulse and respiration rates. Nothing has been mentioned about evidence of a diminution in the fluid in the pericardial sac because for the last fifteen years I have never met with an extensive effusion dangerous in itself, and equally important I have not seen in the post-mortem room a case in which any indication for paracentesis pericardii was present and the amount of fluid had only added a tithe to the great cardiac dilatation. In the adult, carditis is rarely so severe as in the child, but the elements of prognosis are similar and perhaps more frequently there may be considerable pericardial effusion, although this has not been my experience.

The prognosis of the valvular disease cannot be separated from a study of the myocardium. In recent years a distinction has been made by some authorities between valvulitis and endocarditis. It is doubtful whether this distinction is sound, for if by the endocardium is meant the lining of endothelial cells, these cannot be inflamed for they contain no blood-vessels, and if it includes the sub-endothelial connective tissue it is a valvulitis: it is marginal only as distinguished from inflammation of the entire structure of the valve in mitral stenosis. Herein lies the difference in prognosis, that marginal endocarditis with a strong myocardium will heal and patients make in many cases good recovery and become eventually able to live good lives, for the margin of the valve is alone affected. Even then, if the myocardium is seriously damaged, these cases of mitral insufficiency do badly and compensation may never be established.

About mitral stenosis we need more knowledge. We require further prolonged and close observation to ascertain how frequently it slowly progresses, and how frequently it is arrested at a comparatively early stage, and this inquiry should be one result of special convalescent precautions for rheumatic children with the prolonged supervision it implies. If symptoms of mitral stenosis are definite before twelve years the outlook is bad. Tracing such patients we find early deaths, and many less severe die about the fortieth year.

The combination of aortic and mitral valvulitis is always serious when the aortic lesion predominates, and it is my experience that such cases are liable to develop malignant endocarditis in early adult life. If the mitral lesion is predominant recovery may be good and the aortic lesion sink into insignificance. When the myocardium is affected out of proportion to the valvular damage, the patient may drift into a more or less chronic invalidism, suffering from tumultuous action of the heart, lack of cardiac reserve on exertion, nervousness, and frequently dyspepsia and flatulence.

In some cases the valves apparently escape damage altogether, but not the myocardium, and then symptoms due to the weakened muscle may be overlooked or misinterpreted as a solely nervous condition. The enlargement of the area of cardiac dullness may be missed, and the irregular action attributed to indigestion. These cases are often very obstinate, and the prognosis as to a return to really good health should be very guarded. Much will depend upon the patient's surroundings, manner of life and employment. When the pericardium has formed many external adhesions and the heart remains dilated the outlook is also serious.

It should be realized that many cases of rheumatic heart disease are not severe and these tend to improve and do well provided there are not further attacks.

TREATMENT

The treatment of severe acute rheumatic carditis in a child requires much detail, great care and excellent nursing. Taking the long view, it is unsatisfactory; taking the short view, remarkable recoveries may occur and sometimes these recoveries are more successful than the most optimistic could hope to obtain, and negative the long view. The unsatisfactory element in treatment is that no drug appears to control the heart disease. Long experience with the salicylates has led me to great disappointment as to their specific effects, and to believe that pushed in large doses they may do much harm by causing severe vomiting, great depression, and even death from a coma strikingly akin to diabetic coma. With Hanzlik I am doubtful of the value of the combination of double the dose of sodium bicarbonate which, if the dose of sodium salicylate is considerable, means large and depressing doses of the alkali. I have certainly had more successful results with other methods in the most severe cases and venture to write this from an exceptional experience.

Much detail is required in treatment. The patient is usually very nervous, and some children have intervals of panic. Not only is the heart affected, but massive collapse, especially of the left lung, may complicate the case, as also sometimes pleurisy with effusion and a broncho-pneumonia. Sleeplessness and inability to take nourishment add to the difficulties.

Much care is required both in examination and in deciding which symptom is at the moment most urgent. Is it pain? Is it vomiting? Is it sleeplessness? Is it the supervention of chorea or some unexpected collapse? There should be no waiting until there is friction to diagnose pericarditis, for severe symptoms combined with acute dilatation and a persistently rapid and excited action of the heart are all-sufficient and may precede pericardial friction for more than a week. Again, a false step such as exploring the pericardium or pleura needlessly may turn the balance against the patient.

Excellent nursing is required to move the patient with the utmost gentleness, to soothe and calm his fears, to persuade him to take food and medicine, and to be philosophical through a long and finally tedious period of recovery. No case requires more skilled nursing than a child with severe carditis, and adults also need the closest and most discerning attention, for it is a condition in which there may be much pain and mental distress and, if there is also severe polyarthritis, the most utter helplessness.

The best results with carditis, until some specific remedy is found, are gained by carrying out the most minute details with the least disturbance of the patient, for in a severe case there always comes the period when life is hanging in the balance. Either the illness takes a slow turn for the better, or it becomes overwhelming. The turn for the better is always slow and never dramatic as the crisis of a pneumonia. Long experience teaches that the less disturbance there is of the patient the better the chances of recovery, and that hurried, violent or painful treatments are ill-borne. There should be much insistence upon complete rest, preferably with the head and shoulders slightly raised and not, as is often prescribed, with the patient absolutely flat in bed. When very ill the bed may be screened, but as a rule children in a ward feel more comfortable and less alarmed when they can see the nurses and doctors moving about at their duties. Sometimes they must be propped up, at other times they turn almost on their faces, a disturbing sign, for it generally occurs in the more severe cases.

Food should be given in small quantities at frequent intervals, and immediate attention given to vomiting, which, apart from the drugs employed, may be due to flatulence and dyspepsia caused, for example, by milk not suiting the case or requiring some dilution. Skilled nurses are of great value in feeding, for persuasion takes a great part. There is very little evidence that any food that is suitable for children is harmful to the rheumatic. No harm is to be expected from chicken broth or well-made beef tea, or from flavouring milk with a little tea if the child prefers it so. When improvement occurs there appears to be no reason for insisting on continual milky foods. Much has been written about intolerance to carbohydrates in adult rheumatism, but I have never seen any reason for a strange diet in the rheumatic heart disease of childhood, and this resolves itself into choosing the most digestible and most welcome articles given in small quantities and with watchfulness.

Brandy suitably diluted is in my experience most helpful during the stage of grave illness. Children take it well as a rule, and if brandy was a " drug," and not " alcohol," much divergent and sometimes acrimonious discussion about its use would disappear.

The temperature in these cases gives more cause for alarm when it is low than when it is high. In the last twenty years the only cases of hyperpyrexia I have encountered were in children with chorea and both recovered with cold sponging. A far greater number of cases with no fever or nothing beyond 99° F. have been met with, sometimes fatal, and all of great gravity when the carditis was severe. There is, as a general rule, no object in attempting to lower the temperature unless the drug or method employed is exerting also a specific influence in killing the disease. If salicylates are used just to lower the temperature they are not needed, for the worst cases have practically no fever and the temperature is accordingly not an index of virulence.

The regulation of the bowels, commenced perhaps with gr. ½ calomel, should be continued by the mildest aperients, for example, magnesia or syrup of figs. For precordial pain antiphlogistine is, as a rule, comforting and effectual, but if the pain is severe and the child reasonably strong an icebag is more helpful when good nursing is at hand. Otherwise the icebag may be found on the abdomen, or may be found to be leaking. They may be employed in alternation, and I have never seen any collapse from their judicious use but often much comfort.

In the most severe cases occurring in fragile children I have in recent years always used tolysin in 5 to 10 grain doses, according to age, in preference to the salicylates, but the drug is expensive. Some think it is ineffectual and others use the routine salicylate of sodium and bicarbonate of sodium and others aspirin. My preference for tolysin is that in my experience no toxic results occur with the dosage used, and no signs of disorder of the liver have been noted, and freed from anxiety about drug complications the other difficulties of the case can be met with more confidence. If salicylate of sodium or aspirin is used I never exceed 10 grains at a dose, and should there be vomiting stop the drug at once.

It is only when considerable doses of these drugs have been given that I have seen the very rare development of sudden acute œdema of the lungs. Only recently I was asked to see a youth of 18 years who had been treated with considerable, but not excessive, doses of salicylate of sodium (gr. xv) every four hours in whom almost fatal vomiting had resulted, which was stopped only with the greatest difficulty. This obstinate vomiting is a feature of intolerance to this drug of which I have seen a considerable number of cases, some of them fatal. Such a complication I have never seen with tolysin, so that we cannot attribute vomiting in salicylate intolerance to the heart disease, for tolysin has been used only in most severe cases. For sleeplessness a dose of potassium bromide at night may be quite sufficient, but if there is general misery and discomfort nepenthe can be given at night or at regular intervals in the 24 hours. In some cases there may be a distressing ineffectual cough, in which case a linctus containing a small dose of hydrobromate of morphine, as in the mist. tussis rubra of the "Extra Pharmacopœia," may relieve this symptom.

There is diversity of opinion as to the value of digitalis for a heart damaged by acute rheumatism, and there is probably little result to be expected from the drug. In small doses it helps, I think, to steady the action and accordingly use it, though should sickness or nausea result I do not persist, believing that it is all important that the child should take food. I have not as yet persuaded myself to risk any new serum treatment though prepared to do so should future advances show their value. Small doses of bismuth and soda may help to arrest vomiting should it commence, but if this is dependent upon extreme cardiac failure success can hardly be expected.

Recovery is slow. In a patient who recovered from the first severe attack, but died three months later from the extreme damage to the myocardium, the partially adherent pericardium showed that there was still exudation which was not absorbed or healed. Every practitioner who has had great experience of these severe cases recognizes that six months' rest will be needed before there is any certainty that the heart has recovered from the active damage. There are cases—not frequent ones—which repeatedly relapse with outbursts of tonsillitis as soon as they show signs of recovery, and we may be driven to remove the tonsils as a result. It is a critical step to take, but the result may justify this. There is no doubt that the removal of tonsils during an active carditis unless of this exceptional kind may lead to a flare-up of the disease which may prove fatal. I have no shadow of doubt that enucleation of the tonsils in rheumatic children is an operation that requires careful thought in each individual case, and that its blind use as a routine is wrong.

In rheumatic carditis of less severity restriction of a child to absolute rest in bed should not be carried out as a mere routine. Again, each individual case must be studied, for there is no doubt that a child kept over long at absolute rest deteriorates in morale and the heart ceases to benefit. Fortunately we have clinical signs to guide us in our judgment. Increase of appetite and weight are the best signs, then follow a steady temperature, a decrease in the rapidity of the pulse, a diminution in the area of cardiac dullness and strengthening of the impulse. We can test the heart by gentle massage of the extremities, and can follow the general routine in use at the West Wickham Heart Home for successive grading of exertion :—

Grade 1. Complete rest in bed.
,, 2. Bed, but allowed to walk to the lavatory and bathroom.
,, 3. Allowed to get up for 2½ hours daily (10 a.m. to 12.30 p.m.).

Grade 4. Allowed to get up for 4½ hours (10 a.m. to 12.30 and 2 to 4 p.m.).
„ 5. Allowed up 7 hours and to walk and run about.
„ 6. Up all day. Breathing exercises and light Swedish gymnastics.
„ 7. Up all day. A mile walk.

Except with the most severe cases of carditis a practitioner cannot go wrong on these cautious lines.

In connection with the question of recovery, the value of the sedimentation rate of the red blood-cells has aroused interest. This increase in rate is not specific for rheumatism, but occurs quite definitely in this condition. Shall we find that a persisting increase in rate, when clinical symptoms are in abeyance, a sure index of the activity of the disease, or, again, shall we find a sudden rise in rate enables us to detect a relapse? Much investigation over a length of time will be needed to settle these questions to which at present I have received confused and sometimes perplexing answers in the wards. In America also there is sufficient doubt about its practical value to demand patience and careful work before arriving at any definite conclusion upon a most interesting line of investigation.

THE PREVENTION OF RHEUMATIC HEART DISEASE

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IN dealing with the subject of the prevention of rheumatic heart disease it is impossible to attempt in the space at my disposal more than a personal view of the questions involved. So many alert minds in England, America and elsewhere are now at work, with fresh thoughts and novel investigations, on the problems of the rheumatic infection that new side-lights are being turned on old questions, and previously accepted views are again in the arena of controversy. For this reason it seems well to start with some fundamental points on which the prevention of heart disease in rheumatism must be based and to notice some more novel views which have a considerable bearing on the subject.

The pathogenesis of rheumatic heart disease has been established in its fundamentals by the lifelong work of Dr. Carey Coombs, whose recent death is such a great loss to those working at the problems of juvenile rheumatism. The histo-pathological changes in the heart give clear evidence of certain facts. First, the heart is not merely poisoned by some toxin manufactured at a distance, but is invaded in each and every part by living infecting agents. If this is so it follows that acute rheumatism is a blood-stream infection, and the balance of evidence is much in favour of the view that the heart structures are attacked through the coronary circulation. Secondly, the infection for the most part readily subsides and is followed by periods of quiescence and, only too often, of recrudescence. In this respect the histo-pathological evidence is quite in line with clinical experience. Where slowly progressive damage appears to occur in rheumatic heart disease as, for instance, in the establishment of mitral stenosis, healing processes are largely at work. Lastly, the infecting agent produces in the invaded organs a tissue reaction which is practically peculiar to itself; this fact is again well supported by clinical experience, for no disease breeds more true than does juvenile rheumatism. It should, however, be granted that the evidence in favour of the "specific" nature of the infection comes entirely from its behaviour within the body, and that this does not necessarily imply that in laboratory tests the same peculiarity of behaviour will hold good.

As to the actual infecting agent, as everyone knows, the streptococcal origin of acute rheumatism has been on trial for over thirty years. At the present time it may be truthfully said that as a hypothesis it now stands without any serious rival, and that all modern research work on the disease has been founded upon the truth of this view. Personally, I have for many years regarded the proofs of the streptococcal origin of the disease as sufficient, and it must be admitted that this hypothesis has had a longer life than many so-called scientific facts. Curiously enough the outstanding objection to it arises from Coombs's work, though I do not know that at any time he put it forward: it is concerned with the problem how it comes to pass that a streptococcus responsible for rheumatism produces a histological lesion in the tissues so totally at variance with that caused by any other streptococcus.

We are now in a position to examine a few of the more recent hypotheses put forward and having an important bearing on the subject of the prevention of rheumatic heart disease. Clearly anything throwing light on the prevention of the rheumatic infection has a bearing on the prevention of the heart disease which is its essence.

Infectivity and infection by hæmolytic streptococci.—Under this heading there are two hypotheses for consideration: first, that acute rheumatism should be regarded as mildly infectious and so capable of being spread by droplet infection; and secondly, that hæmolytic streptococci play a large part in the production of the acute attacks of the disease. They are considered together here for reasons which will be apparent later, but it must be understood that the two views were not put forward by the same workers, nor sustained by the same arguments. It has been generally held that in rheumatism there is an infection by a non-hæmolytic streptococcus, and one which is normally present in the alimentary tract. How such a streptococcus takes on such a pathogenic rôle is somewhat of a mystery. It may be thought that the micro-organism becomes exalted in virulence in the tonsils or elsewhere, and reaches the blood-stream in a condition which Coombs called one of "parvenu pathogenicity." On the other hand, the resistance to the infection may be worn down, and clinically the occurrence of mild symptoms for some weeks before an acute attack is a common phenomenon which may suggest such an explanation. Even if both these factors be at work, it is clear that in this conception there is little room for the hypothesis that the disease is due to infection by a micro-organism introduced from outside and capable of being acquired from another patient with the same disease. The view that acute rheumatism is infectious is not of any great practical importance, for it is admitted that its infectivity is very low; but it will be seen that its acceptance would require a considerable alteration in our views on the infective agent.

The question of the possible infectivity of acute rheumatism is not a simple one. It is well recognized that fresh rheumatic infection may be set up in a rheumatic child as a sequel to an attack of some non-rheumatic infection. Scarlatina is the best example of this. An outbreak of scarlatina in a ward full of rheumatic children will certainly be followed by many recrudescences of rheumatism amongst them. Yet clearly, though the scarlatinal infection may spread from one child to the next, there is no evidence of the transmission of the rheumatic infection itself. Now, in just the same way, various epidemics of sore throat and catarrh may cause rheumatic symptoms to appear in children who are predisposed to rheumatism. These infectious catarrhs cannot be recognized and labelled with the same certainty as in the case of scarlatina, but that is not to say that they are in themselves necessarily rheumatic. On the present evidence it still seems to me that there is no need to invoke a questionable mild infectivity in order to explain the facts, particularly when the acceptance of such a view would disturb our present ideas of the bacteriology of the disease.

The work supporting the hypothesis that rheumatic infection is due to a hæmolytic streptococcus rather than to the more usually accepted non-hæmolytic variety may be considered here, as most of the investigations in support of this view have been undertaken in connection with outbreaks of rheumatism in rheumatic wards or families. In so far as this is the case, it will be seen that we are not free of the difficulty mentioned above, namely, that non-rheumatic infections may set up rheumatic attacks in predisposed children. Further, much of the evidence linking rheumatism with a hæmolytic infection has been of an indirect nature, such as the examination of throat swabs and fæces, and the investigation of skin and agglutination reactions. Examination of the literature gives the general impression that little direct evidence by means of positive blood cultures has been put forward in support of this view; whereas the non-hæmolytic streptococcus, which has had such a long struggle to win recognition, has been repeatedly found in blood cultures from rheumatic patients. The work on the hæmolytic infection in rheumatism by Paul in America, and by Collis and Sheldon and others in this country, throws a most interesting side-light on the rheumatic process, and is of obvious importance in its bearing on the prevention of rheumatism and so of heart disease. Although it seems questionable if it will be able to upset our conceptions of the infecting agent in this disease, it will in the future be doubtless made to fit in with the rest of the rheumatic picture, and already its practical importance is obvious.

Allergic hypothesis.—This is another recent view, which, if proved correct, will have a great bearing on the prevention of heart disease. To appreciate the interest in this conception, it is necessary to go back to fundamental considerations. It has long been recognized that rheumatism is not a mere matter of a child meeting and becoming infected by a micro-organism: there is much more to it than that, especially if the infecting agent be rightly regarded as a normal inhabitant of the alimentary tract. We are faced by such questions as why does one child get rheumatism when others do not, and more particularly why is it almost impossible to get a rheumatic child to develop a reliable immunity against the disease? The latter point is clearly of immense practical importance and has received added emphasis of late years by the experience of "heart homes." In these the children are cared for in excellent surroundings for months or even years, and regain in many cases first-class constitutional condition: yet it is found that even this cannot ensure them against fresh and severe recrudescences of rheumatism on their return to their homes. Why this should be is not entirely understood. It has been vaguely thought that in some way the child's "resistance" to the infection is diminished, and mention has already been made of the sequence of events which seems to suggest that there is a gradual lowering or wearing out of resistance preceding an acute attack.

It is now suggested that the process at work is not so much a lowering of resistance as the establishment of sensitization in an allergic sense. This view has been put forward in this country by Schlesinger, though allusions to its possibility will be found in Poynton's earlier writings. In support of it is urged the importance of the latent period between the occurrence of acute tonsillitis and the appearance of the other manifestations of rheumatism. That there is usually an interval of ten days or a fortnight between the initial sore throat and the systemic evidence of rheumatism is a very old observation: it is the interpretation of its significance that is novel. It is suggested that this latent period is analogous to that between the injection of antitoxin and the appearance of serum symptoms: in other words, that during this interval, the child is becoming sensitized in an allergic sense. This hypothesis would be more attractive were rheumatism a mere matter of skin eruptions and joint effusions, but it is well known that rashes are rare, and it is generally thought that the arthritis is due to a bacterial infection of the joint. However this may be, it is quite certain that fresh carditis is the result of a fresh infection of the heart due to a fresh bacteriæmic systemic infection, and it is not clear, at all events to the present writer, that allergy can properly be made to include such a process. Although, therefore, there is a need for some additional factor to explain the observed sequence of events in infection by rheumatism, it does not seem that allergy provides a satisfactory explanation as yet. It will be interesting to see if, as our knowledge of allergy increases, its action will be expanded so as to include actual bacterial invasions. Failing this, its part in rheumatism will remain very small and perhaps confined to the explanation of rheumatic erythema, a manifestation of rheumatism whose appearances and disappearances seem to connote very little in terms of active or quiescent rheumatic infection.

PREVENTION IN THE INDIVIDUAL CHILD

The prevention of rheumatic heart disease is, of course, bound up with the prevention of rheumatism. In general, heart disease is not the first of the rheumatic manifestations: it tends to accompany the later and more severe forms of the infection. As a rule, though there are sad exceptions, the graver forms of rheumatism with their added danger to the heart are preceded by weeks or months during which minor and perhaps doubtful symptoms are present. It is during this stage of invasion that there is the best chance of preventing heart disease. Such children tend to fall into different groups. In the first and largest group there are complaints of sore throats and muscular pains. It is far from easy to be sure if such muscular pains are truly rheumatic, especially if they are confined to the lower limbs. Pains occurring in the muscles of the arms, wrists and fingers, or in the neck are likely to be rheumatic. In the second group there are symptoms of nervous derangement which may proceed in time to actual chorea. These will be general nervousness and emotionalism, insomnia, headache, enuresis, tics and perhaps somnambulism. In the third group may be put those cases in which constitutional symptoms are more conspicuous than evidence of local rheumatism. Such children are pale and rather sallow, complain of fatigue, loss of appetite and perhaps shortness of breath. In some there will be a tendency to offensive stools showing the presence of mucus. Taken as a whole, it should be remembered, the rheumatic child is one who looks and is in subnormal physical health. Lastly, there is a group in which the heart gives the first evidence of rheumatism, by showing dilatation, tachycardia or even more advanced damage.

Undoubtedly the early recognition of the rheumatic tendency is the most important measure in preventing heart disease, but as will be seen, the early symptoms are by no means conspicuous or even clear. It must be granted that not all the children with the above mentioned symptoms are truly rheumatic: nevertheless, it is out of such groups of subnormal children that rheumatic cases develop.

Given that the presence of rheumatism is recognized or strongly suspected, the prevention of heart disease lies along some such lines as the following: (1) Regular re-examinations of the child should be carried out for the reason that it is not always obvious to parents how their children are faring in this complaint, and only a proper examination of the heart can detect the early signs of its involvement. (2) Bearing in mind that the general environment of the child is of immense importance, as is shown by the fact that the disease is largely confined to the poorer classes, every effort should be made to provide the patient with good clothing, water-tight boots, warm and dry rooms (especially bedroom), wholesome mixed food and so on. The changing of wet clothes is important. Swimming should, as a rule, be forbidden. (3) Exacerbations of rheumatic symptoms must be strictly treated. The recurrence of pains should be reported to the doctor, and should they be accompanied by any rise in temperature, rest in bed should be ordered. Convalescence should be prolonged and strictly treated in any rheumatic child who catches influenza or other oro-nasal infection. Scarlatina is a special danger to such children: diphtheria and measles are also risks to them. (4) Although some profess to be disappointed in the results of tonsillectomy in rheumatic children, I believe that the removal of infected tonsils is the correct routine in this disease. The earlier the operation is performed the better are its results likely to be. For a week before the operation the child should be under strict observation: evening temperature readings should be taken and the child should be ordered a mixture of potassium chlorate and sodium salicylate to be taken regularly three times a day. With these precautions the risk of an acute exacerbation after the operation is very slight. (5) Lastly, salicylates should be given regularly in small doses over long periods. For this purpose the most suitable is aspirin in doses of 5 to 10 grains night and morning.

The prevention of heart disease in a rheumatic child is, as has been seen, a matter of rather dull routine spread over a very long period. It needs, in a rather special degree, the co-operation of parents: this has been obtained in the case of tuberculosis, and there is no reason why the public should not be educated on the same lines with regard to rheumatism. Although disappointments will be experienced, it seems on the whole that such prolonged care and supervision of rheumatic children are well worth carrying out in an endeavour to prevent heart disease.

ANGINA PECTORIS, SPASMODIC OR PAROXYSMAL

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SINCE 1772, when Heberden gave his classical description of angina pectoris, much ink has been spilt in the discussion of this common, grave, and often lethal disease. It is, however, only in recent years that a clear and valid conception of the pathology underlying the characteristic pain of angina has emerged and found general acceptance. This advance in knowledge has been hastened and assisted by the recent recognition of the identity of coronary infarction and the status anginosus of the older writers. For this material advance we are indebted to Herrick, Pardee, Lewis, Levine, Parkinson and others.

Coronary infarction with its anginal pain is a cardiac accident. Anginal pain of the spasmodic type, on the contrary, is not in the true sense an "accident," but rather evidence of temporary inadequacy of function. Recently Thomas Lewis[1] has investigated anginal pain and has shown that the essential factor is muscular ischæmia. When the blood supply fails to meet the immediate demands of the heart muscle, then pain appears. Muscular contraction liberates certain bodies which give rise to pain if they are allowed to accumulate beyond a certain point. Pain becomes inevitable when the coronary circulation is unequal to its task of flushing the myocardium.

Two factors, then, are clearly involved in anginal pain—the amount of work performed by the heart and the quantity of blood flowing through the coronaries. If the work exceeds the supply then there is a relative ischæmia and pain. It is obvious that any narrowing of the coronary arteries in any part of their course and from whatever cause will diminish their power to meet extra demands for an increased supply of blood. If the supply does not meet the demand, pain ensues.

In addition to the above factors in the production of anginal pain, there is yet another to be considered (which has an important bearing on treatment), namely, the glycogen metabolism of the myocardium and the occurrence of nutritional disorders. Much of the energy of the heart is derived from the combustion of glycogen. This in its turn is dependent on an adequate supply of blood-sugar or on the capacity of the myocardium to utilize available glucose. It has been shown that hypoglycæmia predisposes to anginal pain, and Shirley Smith[2, 3], makes out a strong case for the view that any defect in the glycogen metabolism is a potent factor in the production of anginal pain, irrespective of the presence of coronary disease: though this nutritional factor will induce pain much more readily in the presence of an impaired coronary circulation.

Angina pectoris is an arresting form of cardiac pain, substernal rather than submammary, in which the patient is conscious of a sense of oppression or constriction which may reach a high grade of intensity up to intolerable anguish. This pain has well-recognized lines of radiation and is often induced by effort or emotion. There are in addition characteristic associated symptoms not invariably present, notably the sense of impending death and of acute misery accompanied by varying vasomotor disorders such as cold sweats and deathly pallor. There are all grades of severity from mortal anguish to vague uneasiness with apprehension.

ETIOLOGY

On the etiological side angina is more common in those families with an inherited tendency to arterial disease and hyperpiesia. It is rare in those who have not reached middle age and is commonest in males between the ages of 50 and 70. Good living, lack of sufficient exercise, and excessive mental strain tend to induce that habit of body liable to anginal attacks. Diabetes is an etiological factor of moment because of the high incidence of generalized arteriosclerosis in such patients, and the increased liability to coronary sclerosis. Syphilis, by causing aortitis, stenosis of the mouths of the coronaries and aortic regurgitation, is the determining factor in a number of patients. In such a patient the bulk of the ventricles is great, the orifice of the coronary or coronaries is narrowed, and the diastolic pressure is low, a combination well fitted to produce ischæmia of the myocardium. And when, as is common in this condition, there is a special tendency to localized coronary spasm, we have a splendid example of the factors underlying spasmodic angina.

The essential conditions, therefore, which are responsible for spasmodic angina are to be sought in the coronary arteries, namely, changes which prevent an adequate supply of blood to the myocardium, i.e. a narrowing either at the coronary orifice or in the course of the artery and this latter may result either from organic defect or from temporary spasm. It is of interest that angina is rare in patients suffering from mitral stenosis and in those whose auricles are fibrillating. A well-marked typical example of spasmodic angina can hardly fail to be recognized, but hesitation in diagnosis is sometimes noticed when the anginal pain is slight or characterized by an unusual distribution. The ominous significance of such milder or atypical anginas is none the less certain and it is imperative that these pains should be assessed at their true value. The essential characteristic is that the substernal discomfort or pain occurs in response to effort and is relieved by rest. A repetition of the effort and pain is again induced. There is something sinister about a substernal pain which invariably appears on reaching the same fixed point on ascending an incline—at the same lamp-post, so to speak—and even more ominous when this distance, covered in comfort, steadily diminishes, when the 200-yard man becomes a 50-yard man.

Many patients show a disinclination to use the word "pain" when describing their symptoms, preferring such terms as "dull ache," "sense of oppression," "tightness," "constriction," "a feeling of weight," sometimes merely "an emptiness" or a sensation of "heat or burning." These varied forms of discomfort are usually sternal in site, ranging from the manubrium to the epigastrium, though more commonly in the middle or the upper third of the sternum. When towards the lower third or over the xiphisternum they are often labelled "indigestion," and as these patients not uncommonly develop the habit of aerophagy there is the additional feature of repeated attempts "to bring up the wind," during which air is swallowed and finally eructated noisily with undoubted relief to the patient. This erroneous diagnosis receives still further support from the fact that any exercise following immediately upon a meal, more particularly breakfast, is extremely prone to precipitate an attack.

Anginal pain is neither stabbing nor intermittent. It is steady and continuous and has a crescendo and diminuendo quality, increasing in intensity if the effort which induced it is continued, and tending to cease when the patient rests. This applies equally to those sensations of discomfort, substernal in site which have already been mentioned and which the patients have described in terms other than that of pain. Exposure to cold and emotional disturbance increase the liability to anginal pain, and this is much more noticeable in some patients than in others. In addition, there are frequently numbness and tingling in the arm or fingers, or a dull neuralgic ache is felt above the level of the elbow or in the wrist, more often in the left than in the right. Other areas involved are the left scapular region, the neck, and jaws. In the less obvious cases of anginal pain the occurrence of symptoms such as the above is of great help in assessing the significance of the sternal discomfort.

In patients suffering from pain of an anginal type, physical examination is sometimes disappointing. There may be few, if any, clear indications of disease, and well-marked emphysema, when present, makes the investigation still more difficult. In the hyperpietic enlargement of the heart and an accentuated aortic second sound are to be expected, and in cases of syphilitic aortitis with aortic regurgitation the usual physical signs are easily demonstrated. In many instances, however, no gross deviation from the normal can be made out, and there is a danger that the significance of the pain and other symptoms is then under-estimated or misinterpreted.

On reviewing the past history of patients suffering from angina pectoris, it is found that usually the earliest manifestations were slight and their significance not appreciated. There may be nothing more, perhaps, than substernal discomfort on effort, a sense of weight or oppression, a constriction or feeling of "wind." Gradually these become more and more easily induced by exercise or excitement until there is the typical and characteristic pain, its degree and intensity bearing a definite relationship to the severity of the effort, and tending to disappear with rest.

Another and smaller group begins in a more dramatic manner. In these patients there has been freedom from all discomfort or pain until the onset of coronary infarction. From that time on there is liability to angina of effort. If the coronary infarction has not been severe, the nature of the attack may be missed. It should be suspected whenever anginal pain suddenly attacks an apparently healthy individual, more especially if it occurs when he is asleep or resting. Such a diagnosis is more likely to be correct if the pain or paroxysms of dyspnœa persist for an hour or more, and do not subside with rest, and fail to be relieved by vaso-dilators. As the heart recovers from the infarction the liability to angina of effort may steadily diminish, although it rarely disappears. Recognizing that disease of the coronary arteries is the pathological basis in patients exhibiting effort angina, it is obvious that thrombosis is not an unlikely accident.

PROGNOSIS

At the best there is inevitably an element of uncertainty in the outlook. There is always the possibility of sudden death, due in some cases to coronary thrombosis. In the hyperpietic group vascular accidents, cardiac failure, or renal damage may cut life short. The prognosis is more favourable when there is no history of previous coronary infarction. A well-defined familial tendency to angina and essential hyperpiesia increases the gravity of the prognosis. With such a handicap the expectation of life rapidly lessens after the age of 50 and the appearance of angina on effort is exceptionally ominous. The average expectation of life, excluding cases of coronary thrombosis, is about five or six years, but some patients far outlive this term and it is always wise to defer any opinion concerning the future until the patient has been under observation and treatment for some months. Raised blood-pressure in itself does not appear to be an adverse finding unless it is excessive and associated with indications of renal disease. The future depends not only on the integrity of the coronary arteries and the myocardium, but also on the willingness of the patient to co-operate.

The quality of the myocardium and the extent of the coronary damage can be determined roughly by the degree of effort required to induce pain. Pain induced by walking quietly on the flat is more significant than pain which only appears when the patient hurries. A steady diminution in the amount of effort required to bring on pain is an index of progressive depreciation. The intelligent co-operation of the patient is essential. This may be difficult to obtain when the subjective manifestations are slight or erratic in type. The outlook is much less satisfactory if the patient refuses to accept the diagnosis and submit to the necessary limitations of his activities.

The intensity of the pain may mislead. Patients with a high threshold for pain (the hypo-sensitives) do not experience the same distress as those less fortunate in whom the threshold is low. The type of individual must, therefore, be taken into consideration in assessing the significance of the subjective distress. Certain features are unsatisfactory. The most important is a steady diminution in the amount of effort required to induce pain in spite of a carefully regulated life. The appearance of pain when the patient is at rest is still more ominous. Indications of cardiac failure are of a serious import. When effort, instead of inducing pain, causes dyspnœa, the outlook is definitely worsened. It is significant because it indicates that less effort than is required to induce pain is sufficient to cause shortness of breath. This tendency to dyspnœa is increased by the onset of auricular fibrillation, and though the patient may be troubled no further with angina his days are numbered. Gallop rhythm and pulsus alternans are occasionally observed and are unquestionably adverse features.

An electrocardiogram may yield helpful information.

A low voltage in all leads, the presence of a branch-bundle block, or an abnormal Q R S complex, or evidence of a previous coronary thrombosis, would be unsatisfactory findings suggesting the presence of myocardial damage and to that extent adding precision to the prognosis. On the other hand, an electrocardiogram may yet be within normal limits in patients suffering from well-marked anginal attacks.

TREATMENT

During an attack.—It is imperative on the first indication, even if that be no more than a substernal discomfort or some erratic pain known to be the precursor of an attack, that the patient should cease walking or the work of the moment. The pain is a peremptory order to halt. If the pain does not disappear but increases in spite of rest, one or more tablets of trinitrine should be chewed slowly. These may in turn yield no relief, and then the inhalation of amyl nitrite is essential.

If the vaso-dilators fail and the pain is intense, there is no drug comparable to morphine. It is important that the pain should be eased and morphine must be injected in doses large enough to make the patient comfortable. If, however, the pain proves very resistant and recurs with increasing intensity in spite of rest and opiates, a coronary thrombosis should be suspected. In the less severe attacks, the flatulence of aerophagy may be a distressing symptom, and this is generally relieved by a mouthful of neat brandy or a strong carminative draught, such as the following :—

℞ Mentholis	gr. viii
Spts. ammon. co. Tr. card. co. Tr. zingiberis	āā ℥ 1

Sig. : Two teaspoonfuls to four tablespoonfuls of water.

During periods of increased liability to anginal attacks a mixture containing opium and chloral given twice daily undoubtedly diminishes this tendency. In the angina associated with aortic regurgitation nocturnal attacks are common. Here again, a draught of opium and chloral taken last thing at night proves effective.

Every patient learns by experience the special activity or combination of circumstances liable to induce an attack, and his common sense teaches him to avoid them. Certain forms of exercise are more likely to induce pain than others. In some there is a peculiar idiosyncrasy for which there is often no satisfactory explanation. It has been noticed that a form of exercise which is boring is more liable to induce pain. Haste and hurry immediately after a meal, more particularly breakfast, are among the commonest exciting factors, and the distress is greater and more quickly induced if he finds himself in a nipping and an eager air. In fact, some persons are so peculiarly sensitive to sudden changes in temperature that even the chilly atmosphere of a fireless bedroom or the contact with icy sheets precipitates an attack. These factors can be avoided. It is noteworthy that some patients have by experience found that if, when the pain first appears, they persist (though more quietly) in their walking the discomfort subsides, and they are able to continue without distress. They have warmed up to their job and the circulation has adapted itself: they have got their second wind. I see no objection to this if repeated trials have proved that this can be done with impunity. On the whole this feature is favourable. Walking and talking simultaneously is often a combination which induces pain. In others, excitement or irritation are especially dangerous. Such patients must cultivate a philosophic outlook and avoid every individual or environment likely to disturb their equanimity.

General treatment.—This is based on the recognition that the circulation through the coronaries is defective and that this defect is permanent and irremediable. Reliance, therefore, must be placed on a change in the mode of life rather than on drugs. The advent of anginal pain is a serious indication that the heart is no longer equal to the demands which are being made on it, and those demands must accordingly be diminished.

As a first step a period of rest is indicated, the duration and completeness of this rest depending on the severity of the symptoms. At this point an opportunity is given for a critical survey of the whole position. A careful investigation should be made not only into the physical condition of the patient, but also into his mode of life and environment, in order to discover the extent of the organic damage, and in what respects he is wasting his energy. A more leisurely life is the aim, but a life in which all vital interests are retained. The pace must be slowed down and the element of hustle eliminated. It is worth while to enquire carefully into the manner in which he spends his time, especially his holidays and week-ends. During the latter, business must be blotted out, and even philanthropic activities given a back place.

Exercise is advisable: the heart muscle must be kept fit. One of the best forms is walking; even golf in the milder cases if the patient is honest with himself and is prepared to cry " halt " if pain appears, though I question whether it is ever wise for an anginal patient to golf in a wind or on a keen cold day. As the condition advances the amount of exercise which can be indulged in with comfort gradually diminishes. It is hardly necessary to mention that in no circumstances should any sudden or severe physical effort be made.

A short rest after each but the lightest meal should be insisted upon, and this is especially important after breakfast when there is often a temptation to hurry off to business. With diminution of the cardiac reserve, many patients find comfort and benefit in retiring early to bed, where they lie placidly reading for an hour or two before settling down to sleep.

Diet is important. Meals should be small, the food simple and digestible, and a minimum of fluid taken with the meal. If the patient is obese then the diet should be such as to bring about a slow loss of weight. Overweight is a serious and unnecessary handicap to the heart. Constipation and flatulence should be avoided. During the period of rest, when the patient first comes under observation, a Wassermann reaction should be carried out and search made for any focus of sepsis, and the presence or absence of hyperpiesia determined. If a raised blood-pressure is present an attempt should be made to determine the optimum pressure for this particular case. This can be done while the patient is under observation, resting, and on a carefully regulated diet. It is futile and unwise to attack a high blood-pressure simply because it is high.

In those in whom there is an outstanding mental factor, the result of prolonged overwork, domestic worries, or financial difficulties, massive doses of ammonium bromide are undoubtedly helpful, prescribed in doses of gr. xx, twice or thrice daily; the addition of chloral hydrate gr. x, twice daily, is valuable. This is especially to be recommended at the beginning of treatment when the patient is facing the revision and reorganization of his life and habits. Later, luminal gr. ½ or theominal gr. v may be administered once or twice daily with advantage, especially in the more restless and eager patients.

In cases of undoubted syphilitic infection potassium iodide in full doses should be given and, if possible, mercury by inunction. Large doses of potassium iodide, xxx to xl grains, thrice daily, are sometimes very valuable in diminishing the nocturnal attacks of angina in patients suffering from marked aortic regurgitation.

Some authorities recommend intramuscular injections of a bismuth preparation in the place of mercury when the Wassermann reaction is positive. I question the wisdom of intravenous injection of the arsenical compounds in anginal patients. There is undoubtedly an element of risk. Boyd Campbell[4] has pointed out that " Unless a patient is prepared to take repeated courses of a salvarsan preparation it is doubtful whether it is well to start at all," and in any case the maximum dose should not exceed 0·45 gram.

Occasionally diathermy diminishes the number and severity of the attacks both in patients with frank hyperpiesia and in those with normal pressures.[5] It is best administered with one electrode placed over the sternum and the other between the shoulders. A suitable dose is from 800 to 1,500 milliampères for 20 to 30 minutes twice or thrice a week. Special care is necessary after toxic illnesses such as influenza. General tonic treatment and hæmatinics are then of value. In those rare cases of anginal pain in patients suffering from pernicious anæmia, the treatment is that of the anæmia. Shirley Smith[3] states that he has obtained satisfactory results from the use of insulin and glucose in anginal patients, irrespective of the presence or absence of diabetes. This offers a new line of attack.

In the treatment of angina pectoris, apart from the actual attacks of pain, it cannot be too strongly stressed that it is essential to remodel the manner of life, to delete unnecessary expenditure of energy, and to live within the limitations imposed by the damaged heart. Dependence must not be placed on drugs.

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CORONARY THROMBOSIS

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CORONARY thrombosis is a common and serious complication of arteriosclerosis that bears comparison with cerebral thrombosis. The vital arteries of the heart and brain are alike sites of election for atheromatous degeneration which, by narrowing the vascular lumen, paves the way for thrombosis. The necrosis of cardiac or cerebral tissue following vascular occlusion is attended with symptoms of the utmost gravity and may prove rapidly mortal, yet many patients survive these attacks. Coronary thrombosis is a newcomer to medical textbooks, but it has already taken its place among the common and important vascular accidents that can be recognized during life. There is no need to dwell on the historical aspects of our knowledge of coronary thrombosis, which have already been adequately reviewed, but it may be noted that the symptoms were familiar to the earliest writers on angina, and that the pathology was accurately described during the latter half of the last century. The knowledge that coronary thrombosis is often compatible with life and even health, and that it can be recognized during life with certainty in many cases, has only come to us during the last twenty years, and we owe it largely to the work of American physicians and especially to Herrick.[2]

THE CORONARY CIRCULATION

The clinical features of coronary thrombosis are easily understood if considered in relation to anatomy and pathology. The heart muscle is nourished by the left and right coronary arteries, and the usual distribution of these two vessels is illustrated in Figs. 1, 2, and 3. The left coronary divides almost at once into anterior descending and circumflex branches. The left anterior descending branch supplies the anterior wall of the left ventricle, including the apex, the anterior part of the septum, and an adjacent strip of the right ventricle. The left circumflex branch supplies the lateral and part of the posterior wall of the left ventricle. The right coronary supplies most of the right ventricle, the posterior part of the septum, and a considerable part of the posterior wall of the

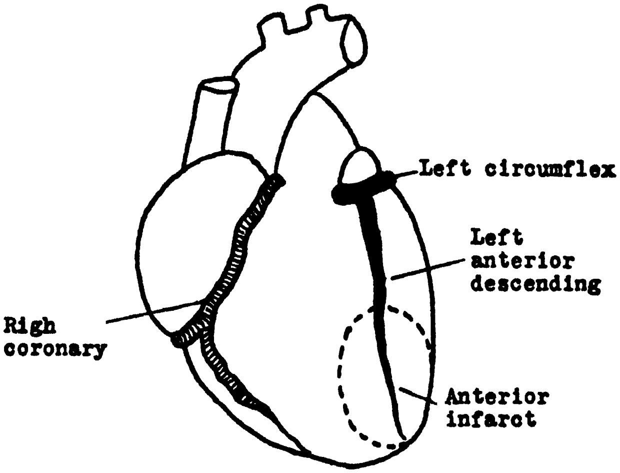

FIG. 1.—Distribution of the left and right coronary arteries on the anterior surface of the heart. The position of anterior infarction, due to occlusion of the left anterior descending coronary, is indicated.

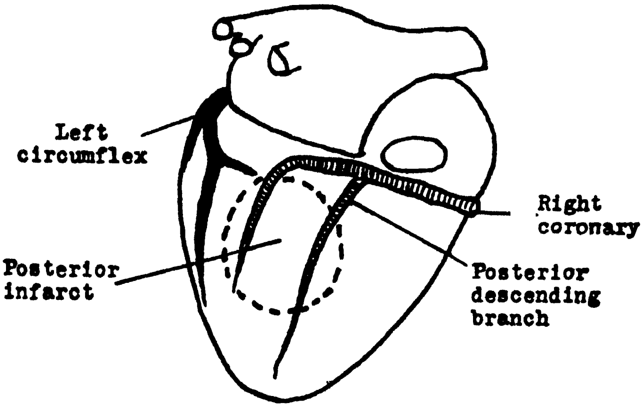

FIG. 2.—Distribution of the left and right coronary arteries on the posterior surface of the heart. The right coronary supplies the posterior wall of the left ventricle. The position of posterior infarction, due to occlusion of the right coronary, is indicated.

left ventricle. Thus the blood supply of the posterior part of the left ventricle is shared between the right and left coronary arteries, and varies considerably in different hearts.

Cohnheim and others taught that the coronaries were "end-arteries," and that anastomoses between their main branches, if they existed, were scanty and limited to the terminal twigs. Spalteholz and later Gross and others have demonstrated, by means of injections, that there are free and abundant anastomoses in the heart muscle, between the larger coronary branches. In addition, there is a copious network of vessels in the subpericardial fat, which provides for free communication between the main coronary trunks. Finally, the coronary capillaries communicate directly with the heart cavities by means of the Thebesian vessels. As age advances, the anastomotic channels in the left ventricle increase considerably, so that the senile heart is prepared to cope with arterial obstruction.

Coronary occlusion and cardiac infarction.—The predisposing cause of coronary thrombosis is almost always stenosis of the vessel lumen by atheroma. In rare cases embolism may be the cause of sudden coronary occlusion. Syphilis scarcely ever affects the coronary trunks, and does not play any part in coronary thrombosis, though atheroma and thrombosis may occur in syphilitic cases. Occlusion of the coronary orifices may be due to syphilitic aortitis or to aortic atheroma, but the process is gradual. The effect of coronary occlusion on the myocardium varies considerably, depending on the rate of occlusion, on the age-changes in the intra-myocardial anastomoses, and on the condition of the remaining branches. Gradual occlusion permits the collateral circulation to develop so that the myocardium may suffer little or no damage, but sudden occlusion leads to serious anæmia of the muscle supplied, part of which is likely to be damaged beyond repair. The effect of sudden occlusion is less serious when it involves a branch already almost closed by atheroma, as the collateral channels will have developed. When coronary atheroma is severe and generalized, a collateral circulation cannot function properly and ischæmic fibrosis and even acute infarction may occur in the absence of thrombosis. From these considerations it is easy to understand why the symptoms of coronary thrombosis vary so much in severity in different cases. The process of infarction following sudden coronary occlusion consists of anæmic necrosis with a variable amount of hæmorrhage and exudation. The necrotic tissue separates gradually, is surrounded by granulation tissue and absorbed, its place being finally taken by fibrous tissue. Fibrous replacement probably requires about five to eight weeks. The infarct rarely involves the whole thickness of the ventricular wall, and is usually confined to its endocardial aspect, the outer layers of muscle being preserved by the subpericardial vascular network. During the first three weeks, while the infarct is still friable, rupture may occur. A thrombus may form on the inner surface of the infarct, within the ventricle, and is likely to become dislodged and cause embolism. When the septum or apex is involved, clots may form in both ventricles, so that pulmonary and systemic embolism follows. Fibrinous pericarditis sometimes develops on the outer surface of the infarct and may be sufficient to produce pericardial friction sounds. The process of absorption of an infarct is usually accompanied by mild fever and leucocytosis for about a week. Complete healing of the infarct leaves a shrunken fibrous scar, sometimes with pericardial adhesions. It may gradually yield to form an aneurysm of the ventricle. Rarely an old infarct becomes calcified.

The commonest site for coronary thrombosis is the left anterior descending branch, near its origin, but the right coronary is quite frequently involved[1]. Infarction is almost limited to the left ventricle, the right ventricle scarcely ever being involved except where a left ventricular infarct overlaps it. There are three common geographical types of infarct, corresponding to occlusion of the main coronary branches (Fig. 3): (1) *Anterior infarction* (left anterior descending coronary) involves the lower part of the anterior wall of the left ventricle, the apex, and sometimes adjacent portions of the septum and right ventricle. (2) *Posterior infarction* (right coronary) involves the upper part of the posterior wall of the left ventricle and sometimes adjacent portions of the septum and right ventricle. (3) *Lateral infarction* (left circumflex coronary) involves the lateral wall of the left ventricle about its middle.

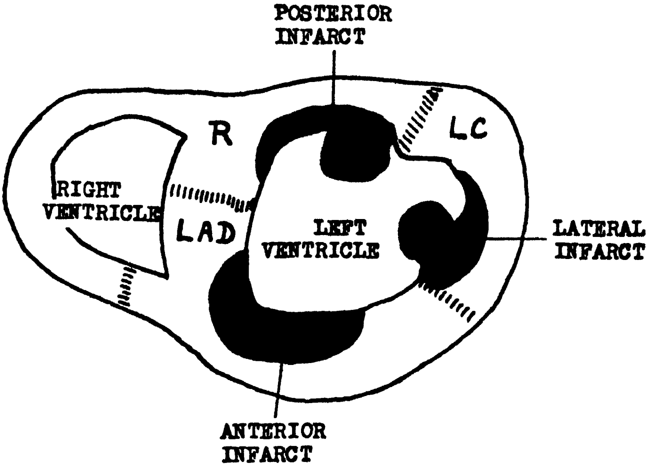

FIG. 3.—Cross-section of the heart, showing the areas supplied by the left anterior descending branch (LAD), the left circumflex branch (LC), and the right coronary (R). The position of the three common types of infarct is indicated.

Functional disturbances due to coronary thrombosis.—The sudden ischæmia of a zone of cardiac muscle which follows coronary occlusion often gives rise to intense anginal pain. The infarct itself need not be painful, for by the time it has formed the pain has often ceased. It is not dead muscle, but impaired or dying muscle that is painful. Sudden ischæmia may disturb the normal rhythm of the heart, or interfere with conduction. The onset of ventricular fibrillation probably accounts for sudden death at the start. Short of this, there may be extrasystoles, paroxysms of tachycardia, auricular fibrillation, and rarely heart block with Stokes-Adams attacks. Paralysis of a wide area of myocardium impairs the efficiency of the heart as a pump, so that blood-pressure falls considerably and the output of the heart diminishes. Unless the anæmic muscle rapidly recovers to some extent as the collateral blood-supply comes into play, the ordinary signs of heart failure, such as dyspnœa, œdema of the lungs, and venous engorgement, appear. Thus the three cardinal manifestations of coronary thrombosis are: (1) anginal pain; (2) fall of blood-pressure and collapse; (3) signs of congestive heart failure.

Changes in the electrocardiogram.—Changes in the electrocardiogram follow ligature of a coronary branch in animals, and Pardee[5] and Herrick[3] first recorded similar changes in human curves after coronary thrombosis. Serial electrocardiograms show a series of changes corresponding to necrosis and healing of the infarcted muscle.[7] Fig. 4 shows a typical curve, taken shortly after the onset of symptoms. The T waves take off from the RS waves above or below the zero level, so that the R-T segment is elevated or depressed. Within about a week R-T returns to the base line, and deep inversion of the T waves occurs in lead I or lead III, but not in both (Figs. 5 and

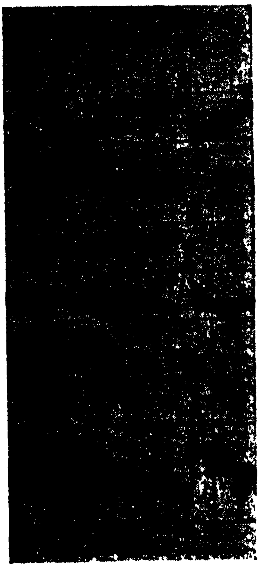

FIG. 4.—Electrocardiogram taken a few hours after the onset of coronary thrombosis. The R-T segment is depressed in lead I, and elevated in lead III. The large Q wave in lead III is common in coronary disease.

6). In the course of a few months, sometimes quicker, changes towards normal occur, and occasionally the curve becomes quite normal. Inversion of T in lead I (T1 type) probably corresponds to anterior infarction, and inversion of T in lead III (T3 type) to posterior infarction.[1] A large Q wave in lead III is frequently observed. Changes in the electrocardiogram are not constant, but they are frequent and of great diagnostic value, especially when serial records can be obtained. It is rare to find the curve remaining normal during the first week.

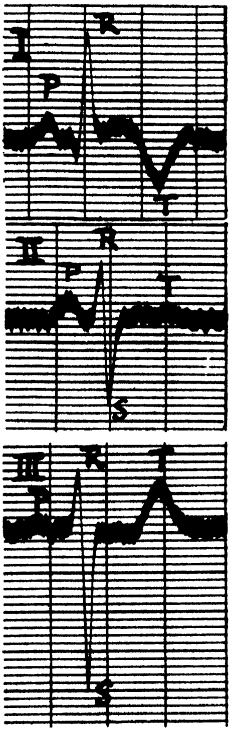

FIG. 5.—Electrocardiogram taken three weeks after coronary thrombosis, showing the T1 type of curve.

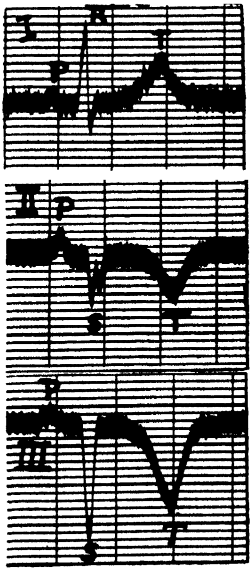

FIG. 6.—Electrocardiogram taken one month after coronary thrombosis, showing the T3 type of curve.

THE CLINICAL PICTURE

Incidence.—Coronary thrombosis is most frequent between the ages of 50 and 70, is fairly common between 40 and 50, and occasionally occurs in the thirties. Men are affected far more often than women; in Parkinson and Bedford's series,[6] 90 per cent., and in Levine's,[4] 76 per cent. were males. About half of them have experienced anginal pain on exertion prior to the attack, though this may have masqueraded as "indigestion" or "rheumatism"; others have had dyspnœa or some degree of heart failure, and some have been free from cardiac symptoms and in normal health. Many have hypertension, and in these the heart is usually enlarged, but if the blood-pressure has not been raised the heart is probably normal in size. The peripheral arteries are often, but not always thickened, and the aorta may show signs of atheroma on X-ray examination.

Symptomatology.—When the onset of coronary thrombosis is marked by an acute seizure, its clinical recognition is not often difficult. Such acute attacks consist of one or more of the three cardinal features of coronary occlusion, namely, anginal pain, collapse, and heart failure, any one of which may predominate. The recognition of these severe anginal seizures as evidence of coronary thrombosis has been a relatively recent and important advance in clinical medicine. Now that the novelty is passing, we should take a wider view of cardiac infarction, and pay attention to the later stages as well as to the onset. Cardiac infarction is a not uncommon underlying cause of ordinary congestive heart failure, or of ordinary angina pectoris of effort. In cases of congestive failure due to cardiac infarction, the history may reveal an acute anginal or dyspnœic episode in the past, the attack may have been mild or unrecognized, or the symptoms may have developed gradually.

Ordinary angina pectoris may date from an attack of coronary thrombosis, or a healed infarct may be found post-mortem in cases of angina in which there has never been a prolonged attack of pain. In another type of case, ordinary anginal attacks are gradually replaced by symptoms of heart failure—the anginous patient becomes a cardiac, as Gallavardin aptly puts it. The following grouping of symptoms is purely for convenience in emphasizing particular clinical features:

(1) *Medico-legal type*: This includes cases of sudden death at the onset of coronary thrombosis, before an infarct has formed, and cases in which the symptoms have been mild and unrecognized, and where death occurs suddenly and unexpectedly. Ventricular fibrillation or rupture of the heart is the cause of death.

(2) *The anginal type*: This includes the majority of cases in which coronary thrombosis is recognized during life. The attack may be summarized as a severe and prolonged anginal seizure, accompanied by collapse and often followed by heart failure. The onset of pain is sudden and not related to exertion, often occurring at rest or during sleep. The pain is sternal, may radiate across the chest, or into the back, arms, neck and jaws. Not infrequently it is located at the lower end of the sternum or in the epigastrium. Signs of shock and collapse accompany the pain; pallor, profuse sweating, vomiting, and weakness are usual. The pulse may be impalpable at the wrist, but when felt is probably rapid, small, and regular. The blood-pressure when first recorded is low, often about 100 mm. systolic, but in cases of hypertension a big drop in pressure may occur without the level becoming subnormal. Dyspnœa is not usually prominent at the onset, but may quickly follow, and breathing may be of the Cheyne-Stokes type. Seen shortly after the onset, a typical patient is restless and distressed, in great pain, the features are an ashen greyish hue, and sweating is profuse. The heart's impulse is feeble, the sounds are distant, and some œdema of the lungs is

very common. As important variations, the pulse may remain normal in rate, may be irregular, or there may be paroxysms of tachycardia. The fall in blood-pressure may be gradual or delayed, and collapse be less prominent than pain. Dyspnœa and œdema of the lungs may dominate the picture. Persistent vomiting, hiccough, abdominal tenderness and distension may occur, and when the liver is tender and enlarged and an icteric tinge is present, an acute abdominal lesion is closely simulated.

After hours, or perhaps several days, the pain subsides or yields to morphine. Slight fever, leucocytosis, or pericardial friction may be observed, tachycardia persists, and the blood-pressure remains low. In favourable cases, as the pain and shock subside, the patient improves rapidly. Recurrences of pain, embolic complications, or a slight degree of heart failure may interrupt recovery. In unfavourable cases, the patient succumbs to persistent or recurrent paroxysms of pain, or severe dyspnœa and pulmonary œdema set in and the condition becomes rapidly hopeless. During the first three weeks, while the infarct is still necrotic, life is always in jeopardy. Sudden death may occur at any time from ventricular fibrillation, rupture of the heart, or embolism, but becomes less likely after the end of three weeks.

(3) *Cardiac failure:* Sudden dyspnœa, œdema of the lungs, and venous engorgement, often accompanied by collapse, but without pain, may mark the onset of coronary thrombosis. Painless infarction appears to be most common in those who already have some degree of heart failure prior to the attack. The association of cardiac infarction and hypertensive heart disease may give a fairly characteristic clinical picture. A patient with severe congestive failure that has developed rapidly is found to have a large hypertrophied heart, with gallop rhythm, a persistently low blood-pressure,

and often recurrent attacks of pulmonary œdema. Changes in the electrocardiogram, or embolic complications may point to cardiac infarction.

(4) *Special clinical features :* (a) *embolism.*—Embolic accidents may overshadow the other symptoms, or may be delayed and perhaps provide the first evidence of past coronary thrombosis. When pulmonary and systemic emboli co-exist, the possibility of cardiac infarction should always be considered. The following is an example :—

A woman, aged 63, was seen in 1930, complaining of pain in the right chest, breathlessness, cough, and hæmoptysis. In 1928 she had been in bed with dyspnœa and pulmonary congestion, but recovered. She was breathless and cyanosed, and there was cough and purulent blood-stained expectoration. The pulse was regular, the heart seemed slightly enlarged, with gallop rhythm at the apex, and blood-pressure was 150/105 mm. There were signs of extensive consolidation at the right lung base, and a radiogram showed opacity of the whole lower lobe. Pulmonary neoplasm was suspected. Electrocardiogram, bundle-branch block. Wassermann, negative. Symptoms of heart failure became evident, and increased. She was seized suddenly with severe cramps in both legs and pain in the hypogastrium ; the limbs became cold, powerless, and insensitive, and gangrene soon supervened. She died ten days later.

Necropsy revealed old infarction of the right lung, and occlusion of the corresponding pulmonary artery by organized clot. The abdominal aorta was completely occluded by a thrombus in its lowest four inches, and a large embolus was identified. The heart was hypertrophied, the coronary arteries were atheromatous, and the left descending branch was completely occluded. There was an extensive fibrous infarct of the left ventricle and septum with organized and recent clot over it, and also ante-mortem clot in the right ventricle.

She probably had coronary thrombosis in 1928 with intracardiac thrombosis which organized. She recovered, but fresh clot formed over the infarct and caused pulmonary and aortic embolism which proved fatal.

(b) *Paroxysmal tachycardia.*—Paroxysmal tachycardia of ventricular type is especially likely to follow coronary thrombosis, and occasionally the paroxysms may be the dominant clinical feature. Anginal pain occasionally complicates paroxysmal tachycardia, apart from cardial infarction, so that diagnosis is sometimes difficult. If an electrocardiogram shows the tachycardia to be of ventricular type, evidence of cardiac infarction should be sought.

DIAGNOSIS

The diagnosis of coronary thrombosis may have to be made at the onset, or retrospectively in cases of chronic myocardial infarction. Acute coronary occlusion must be differentiated from other acute cardiovascular conditions that cause pain and dyspnœa, painful pulmonary conditions, and acute abdominal emergencies. Dissecting aneurysm of the aorta may produce symptoms identical with those of coronary thrombosis, but the distinction is not important. Syphilitic aortitis and aneurysm may cause severe and prolonged pain, but fall of blood-pressure and failure are absent. X-ray examination and a Wassermann test will establish the diagnosis. When syphilitic aortitis constricts the coronary orifices, the clinical picture is often identical with that of coronary thrombosis. Cardiac asthma and acute pulmonary œdema may be accompanied by some oppression in the chest, but they are usually episodes in hypertensive heart disease, and the blood-pressure remains high or rises rapidly with recovery. Pulmonary embolism can produce shock, tachycardia, severe pain, and dyspnœa, and definite signs in the lungs may be absent at the onset, but some cause for embolism may be present, and signs in the chest and hæmoptysis will appear. Pulmonary infarction may complicate coronary thrombosis.

The diagnosis from acute abdominal conditions, such as perforated gastric or duodenal ulcer, acute cholecystitis, and pancreatitis may be most difficult. In coronary thrombosis the pain may be epigastric, the abdomen tender and even rigid, vomiting and hiccough may be persistent, the liver may be tender and slight jaundice be present. The history is most important. Previous anginal pain, related to exertion, or radiating to the arms or neck, points to the heart, while previous pain related to food, gallstone colic or jaundice point to the abdomen. Tachycardia, low blood-pressure, and slight œdema of the lungs suggest a cardiac rather than an abdominal lesion. In any case of doubt, an electrocardiogram may clinch the diagnosis.

Previous coronary thrombosis may often be recognized in cases presenting themselves with heart failure or with ordinary angina pectoris. A careful history will often bring to light a painful or dyspnœic seizure in the past. Low blood-pressure, unexplained embolism, or paroxysms of tachycardia are often suggestive.

PROGNOSIS

Of those patients who survive the onset of coronary thrombosis long enough for the diagnosis to be made, probably about half recover from the attack. The intensity of the pain and the severity of the initial collapse are not reliable prognostic signs. Persistence of collapse, recurrent attacks of pain, and the rapid onset of signs of congestive failure are of serious import. The prognosis during the first three weeks is always uncertain, however well the patient may appear. Those who recover from the attack may live for many years in relative health, and may even continue at work. Others are restricted by anginal pain or breathlessness. By stressing the hopeful aspects of coronary thrombosis, patients and relatives are encouraged, and a period of irksome inactivity may be better tolerated.

TREATMENT

At the onset, morphine is urgently required and should never be withheld, even when there is vomiting. The dosage must be adequate to afford relief from pain, and ¼–½ grain should be given at the start, and a second dose if necessary. Preparations for a long illness, and for nursing should be made without delay.

The bowels may be disregarded for the first few days, when an enema may be given. Warmth is important. Glucose by the mouth and liquid foods are all that is required at first. Stimulants are of no value, but brandy may be comforting. Digitalis is only required if heart failure occurs, or if there is auricular fibrillation, and moderate doses, such as 20 minims thrice daily, should be used. In cases with ventricular tachycardia, quinidine can be tried, provided that electrocardiographic proof of the abnormal rhythm has been obtained. Five or ten grains may be given and repeated in two hours in urgent cases.

The most important part of treatment is an adequate period of complete rest in bed. Two months is to be regarded as the minimum, and if complications occur, or if heart failure is present, this period must be extended. Convalescence should be gradual, and a quiet holiday or a sea voyage is of benefit. The question of future life should be left until convalescence is complete, and the heart's capacity can be tested. While it is often wise to advise retirement, and to restrict activity reasonably, an invalid existence is not likely to prolong life, once the infarct has healed. In the absence of anginal pain, and of dyspnœa, reasonable activity is to be encouraged rather than restricted.

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THE TREATMENT OF CONGESTIVE HEART FAILURE

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THE term " heart failure " means that the reserve power of the heart is reduced to such an extent that the organ is no longer capable of maintaining an output of blood adequate to supply the requirements of the body. These requirements vary in accordance with the mode of life of the patient, and depend chiefly on the amount of physical activity that he is accustomed to undertake. Since physical exercise makes the greatest demand upon the heart, cardiac failure, in its early stages, commonly manifests itself by respiratory distress on exertion. The diminished output of the failing heart leads to a sluggish circulation. The blood remains too long in the capillaries, and its content of carbon dioxide rises to an abnormally high level; this excites the respiratory centre, and so causes dyspnœa. A second result of the sluggish circulation is excessive de-oxygenation of the blood. The amount of reduced hæmoglobin in the capillary blood is increased, and consequently the patient becomes cyanosed. The associated cyanosis assists in the diagnosis between cardiac dyspnœa and dyspnœa due to purely nervous or other causes, such as uræmia and ketosis.

When the cardiac reserves are still further reduced, the heart is unable to dispose of the blood as quickly as it receives it—the inflow exceeds the output—and the venous pressure rises. The patient is then said to be suffering from "congestive heart failure." The presence of venous engorgement can most easily be recognized in the organs in close proximity to the heart—namely, the liver and the lungs. The liver enlarges, moist sounds make their appearance at the pulmonary bases, and the veins in the neck stand out like knotted cords. Venous engorgement of other organs, such as the stomach and the kidney also occurs, but its presence can only be surmised from indirect evidence—nausea, dyspeptic symptoms, oliguria and albuminuria. Lastly, anasarca develops, and fluid may accumulate in the peritoneal and pleural cavities, giving rise to ascites and hydrothorax.

GENERAL PRINCIPLES OF TREATMENT

As in all other conditions, the first indication for treatment is to find out and to endeavour to remove the cause of the trouble. Congestive heart failure may be due to various causes, but in more than 70 per cent. of cases its appearance is directly attributable to the onset of some abnormal rhythm, which interferes with the efficient working of the heart. Of such abnormal rhythms, by far the commonest is auricular fibrillation; and the rational treatment of heart failure in these cases resolves itself into the effective control of the fibrillation. In untreated auricular fibrillation, the heart rate is usually very rapid, and its rhythm extremely irregular. Hence the ventricles are working overtime, they get insufficient rest, become fatigued, and sooner or later dilate. Since many heart-beats follow each other in rapid succession, the ventricles often contract before they have had time to fill with blood. Their output therefore is much reduced, and many beats are unproductive. It is not the paralysis of the auricles, but the ventricular tachycardia that is to blame for the heart failure which so frequently follows auricular fibrillation. The manner in which this can be overcome will be discussed later.

Congestive heart failure with normal rhythm is a much less common condition. It is most apt to occur in old-standing cases of high blood-pressure, and cardio-aortic syphilis, or as a complication of chronic pulmonary disease, such as bronchitis and emphysema. In this group of patients the prognosis is much less favourable than in the fibrillators, for they do not respond in the same way to digitalis or to other therapeutic measures.

A second cardinal principle of treatment is to put the diseased organ at rest. The heart can never rest. The most we can hope to do is to curtail the amount of work which it is called upon to perform by eliminating all unnecessary exertion. This implies that the patient should be confined to bed. If he is dyspnœic even at rest, he must use a bed-pan, and be attended by competent nurses who will feed him, wash him, and lift him when he wishes to change his position. He must not be allowed to make any physical effort, or even to attempt to assist his nurse in moving him. Dyspnœic patients are more comfortable sitting up than lying flat, since this position allows for freer movements of the ribs, and at the same time prevents the engorged liver from impeding the descent of the diaphragm during inspiration. Some patients, especially the obese, find it easier to get to sleep when in a chair and leaning forward with the forearms supported by a table and the head resting on the forearms. Whatever position the patient finds most comfortable should be adopted; and, if in bed, the feet and knees should be supported to prevent him from slipping down. Skilled nursing is one of the most important considerations in the treatment of advanced heart failure, for it is the only means of ensuring complete bodily rest.

Next in importance to physical rest is peace of mind, for a state of mental anxiety is incompatible with complete physical relaxation. Conversely the active mind needs occupation, especially in the less grave type of case. Here psychological considerations predominate and call for tact and cheerfulness on the part of both nurse and doctor. An adequate period of sleep must be secured at any cost. When lack of sleep is due to pain, morphine may be necessary, but often one of the milder hypnotics, such as dial, will suffice; paraldehyde is a safe drug to use in heart cases, but must be given in full doses (i.e. not less than 2 drachms). A " night-cap " of whisky with hot water and lemon is worth trying.

To sum up, when the heart is failing we may be powerless directly to increase its assets, but much can be done to reduce its liabilities. So long as the liabilities exceed the assets the outlook is gloomy; but as soon as the heart can balance its budget, there is ground for optimism. The importance of reducing to a minimum the demands upon the failing heart cannot be over-emphasized. The same applies in a lesser degree to the digestive organs. As engorgement of the mucous membrane of the stomach and intestines renders digestion difficult, the diet should be simple and easily digested.

When the patient is desperately ill, fluid only will be tolerated, and this is best given in the form of peptonized milk, one pint in the twenty-four hours being sufficient. If milk alone is not tolerated, it may be diluted with an equal quantity of lime water, and a few drops of the tincture of iodine added to the mixture. Glucose given with insulin has been recommended in acute heart failure, but opinion is divided regarding the efficacy of this line of treatment. As soon as the patient is able to take solid food, a fairly dry diet is best, thirst being quenched by drinking between, instead of with meals. The meals should be small in order to avoid over-distension of the stomach, and as a corollary, given at frequent intervals. During the day the patient should never go longer than three hours without food, though during the acute stage of the illness the total heat value of the diet need not exceed 1,000 calories.

Dyspeptic symptoms are often troublesome, and may be relieved by an alkaline mixture, such as the following :—

℞	Magnesium oxide	-	gr. viiss
	Bismuth carbonate	-	gr. v
	Ammonium bromide	-	gr. v
	Tincture of belladonna	-	♏ iv
	Spirits of chloroform	-	♏ iii
	Peppermint water	to	℥ i

This should be given 10 minutes before meals, and supplemented when there is flatulence by a carminative after meals in the form of a couple of soda-mint tablets or the following mixture :—

℞	Menthol	- - - - - - -	gr. ¼
	Aromatic spirits of ammonia	- - -	♏ xxx
	Compound tincture of cardamoms	- -	♏ xxx

In place of the usual carminatives, for patients accustomed to take alcohol crème de menthe may be prescribed. Strong tea and black coffee must be prohibited, even during convalescence, but weak China tea and milky coffee are permissible. When persistent vomiting occurs, champagne can sometimes be kept down, but feeding by mouth may be impracticable, and rectal feeding may have to be resorted to. For this purpose a small enema consisting of an ounce of glucose in a pint of saline given four-hourly is preferable to the more complex formulæ which are sometimes prescribed. Obstinate flatulent distension of the stomach can frequently be overcome by this means when all other methods of treatment have failed.

SPECIAL TYPES OF HEART FAILURE

After this consideration of the problem from a general standpoint, it is now desirable to deal with various special aspects of the subject, to which special lines of treatment are applicable.

Auricular fibrillation.—In controlling the ventricular tachycardia, to which heart failure is attributable in this condition, we must rely on drugs of the digitalis group.

In cases of extreme urgency, strophanthin may be given intravenously in doses of 1/100 gr., but, with this single exception, digitalis is the most certain remedy. Strophanthus is still extensively used, but given by mouth it is much less reliable than digitalis, on account of the fact that its absorption from the gastro-intestinal tract is extremely variable. A dose which at one time is barely sufficient to produce any therapeutic effect, will at another time, in the same person, give rise to toxic symptoms.

The method of digitalis administration varies in accordance with the urgency of the symptoms in the particular case, but the general principle holds good for all that in order to produce the desired action on the heart, the patient's system must be fully saturated with the drug. The total quantity required to produce full digitalization varies roughly with the body-weight of the patient (bearing in mind the fact that when there is extensive œdema the actual weight is considerably greater than the normal weight). For a man of 10 stone, about 15 to 20 c.cm. (4 to 5 drachms) of the tincture will be necessary. When the symptoms are not urgent, this quantity may be spread over a period of four or five days, the patient taking 20 minims of the tincture three times a day. There are, however, cases of extreme urgency in which a fatal issue seems probable unless the heart rate can be controlled quickly. Much larger doses (1 drachm 6-hourly) may then be given with safety, provided that certain special precautions are taken. In the first place it must be ascertained that the patient has not been taking any drug of the digitalis group during the preceding three weeks, for if he be already partially digitalized, a single large dose may then produce toxic symptoms. Secondly, it is important to allow an interval of six hours to elapse between successive doses, in order that the full effect of one dose may be observed before the next is given. Thirdly, the drug must be promptly discontinued should toxic symptoms develop; these may be either gastro-intestinal (nausea, vomiting and diarrhœa) or circulatory (excessive slowing of the heart rate, or coupling of the beats). Digitalis acts as a diuretic in cardiac cases, but if given in excessive amounts the reverse is the case, and a sudden diminution in the output of urine suggests over-dosage.

A practical point of importance is that vomiting is a common symptom in congestive heart failure, and does not necessarily imply digitalis intoxication. If, therefore, vomiting occurs when a small quantity only of the drug has been given and the heart rate is still rapid, the treatment must be persevered with, and not discontinued. When full digitalization has been obtained, only a small holding dose is required. This varies in different patients, and has to be determined by trial and error in each case. Sometimes as little as 15 minims in the twenty-four hours will suffice, but other patients need a larger quantity.

The aim of digitalis therapy in auricular fibrillation is to hold the heart rate in the neighbourhood of 70 to 80 per minute. There are, however, two conditions—fever and thyrotoxicosis—in which the basal heart rate is set at a higher level; and it is important to remember that an attempt in these circumstances to force the heart rate down below 100 is equivalent to forcing it below 60 in other conditions, and so to approach the danger zone.

As an alternative to the tincture, the powdered leaf given in tablet form is a useful preparation, 1½ grains of the leaf being equivalent to 15 minims of the tincture. Eight minims of the tincture is equivalent to one of the pink Nativelle's digitalin granules (1/600 gr.). This is a very convenient form in which to prescribe the drug when only a small "holding dose" is required.

On account of the risk of embolism, quinidine has no place in the treatment of auricular fibrillation when congestive heart failure is present. In these patients venous stagnation frequently leads to the formation of clots in the engorged auricles. The resumption of auricular contraction may then lead to the detachment of a portion of the clot and its expulsion as an embolus into the general circulation. There is a second contraindication to the use of quinidine in this condition; congestive heart failure, which is not attributable to an attack of bronchitis or to some intercurrent infection, is usually a late manifestation of heart disease, and it is usually associated with considerable myocardial damage. Many of these cases fail to respond to quinidine, and those which do respond soon revert to fibrillation. Even if normal rhythm can be restored and maintained, the patient is not any better off, since the heart rate is usually rapid, and cannot be controlled like that of the fibrillator by digitalis.

Hypertension.—Many cases of congestive heart failure are attributable to high blood-pressure. In this type especially, venesection may afford immediate relief. When the right heart is embarrassed by the raised venous pressure, a pint of blood should be withdrawn, and the procedure may be repeated if necessary. Regarding the technique of this small operation, a sphygmomanometer bandage is applied to the upper arm and the pressure raised to about 50 mm. The patient is then asked to clench and unclench the fist a few times until the veins stand out. For the puncture, the tapered needle designed by French is a distinct improvement on the ordinary type, since it is less liable to be plugged by blood-clot. It should be inserted bevel side downwards. In fat persons, the vein at the bend of the elbow must be located by touch and not by sight.

Cough.—Pulmonary congestion is often accompanied by a troublesome unproductive cough, which disturbs the patient and may prevent sleep. A pleasant sedative mixture which is helpful in these cases is a linctus consisting of 20 minims each of the syrups of codeine, virginian prune and liquid pine. Reference must be made to congestive heart failure supervening on acute or sub-acute bronchitis. The prognosis in this group is much more favourable than in the purely cardiac cases in which the causal condition is less amenable to treatment. During the past five years the writer has followed through the later months of pregnancy a group of 150 patients suffering from heart disease. During pregnancy the gradually increasing burden imposed upon the heart by the growing fœtus affords an interesting opportunity of observing the limitations of the cardiac reserve in these women. All those with signs of congestive heart failure tolerated pregnancy badly, and the fatalities in this series of cases were confined almost exclusively to these individuals. There was, however, one exception—namely, patients in whom an attack of bronchitis was responsible for the onset of heart failure. There were three such patients in the series, and all did well. Their bronchitis responded promptly to treatment in hospital. The venous pressure returned to normal, and on re-examination six months after delivery, there was not any evidence that the cardiac lesion had been aggravated by the strain through which the patient had passed.

Slight hæmoptysis is common in the early stages of congestive heart failure. It is due to the raised pulmonary pressure, and may be regarded in the light of a safety-valve mechanism. The patient often feels better after it, and special treatment is not needed. In contrast to this is the profuse hæmoptysis accompanying pulmonary infarction, usually a late manifestation of heart failure; this is always of grave significance, and must be treated by absolute rest, sedatives, and, if necessary, morphine.

Emphysema.—When heart failure supervenes in the course of chronic pulmonary disease, oxygen is useful, for in these cases the nutrition of the heart muscle suffers from the general anoxæmia, resulting from defective oxygenation of the blood in the lungs. Similar benefit cannot be expected when dyspnœa and cyanosis are due either to a sluggish circulation or to direct transference of the blood from the right to the left side of the heart, as occurs in some forms of congenital heart disease. In these latter cases the blood passing through the lungs is already fully saturated with oxygen, and the fault lies not in the lungs, but elsewhere. The aim of oxygen therapy is to increase the tension of oxygen in the alveolar air. It has been proved experimentally that this cannot be achieved by the old "open" method with a funnel suspended at a distance of some inches from the patient's face. The simplest effective method for practical purposes is to deliver the oxygen through a small rubber catheter pushed well back into the naso-pharynx, and held in position by a piece of strapping attached to the upper lip. The oxygen should first be bubbled through water, as the dry gas is irritating. A tablespoonful of brandy may be added to the water, so that some of the vapour is carried over with the oxygen. Incidentally, the water-bottle serves as a gauge to measure the amount of oxygen the patient is getting. The gas should pass through the water at a rate of at least five bubbles per second.

Œdema.—Even in advanced heart failure, life may be made much more tolerable by the removal of œdema. In œdematous patients the fluid intake should be restricted to one pint per diem, and a free action of the bowels ensured by suitable purgatives, such as aloin or pulv. jalap. co. (1 drachm). When the heart failure is attributable to auricular fibrillation, a free diuresis often follows the improvement in the renal circulation when the patient is fully digitalized. Baillie's or Guy's pill is a useful preparation in these cases, since it combines the action of digitalis with that of mercury. When digitalis fails, one of the xanthine group of diuretics (such as diuretin, gr. x–xv, t.i.d.), may be tried; while in patients who prove refractory to these remedies, spectacular results may sometimes be obtained with the mercurial diuretics of which the least toxic is salyrgan, which is given intravenously in doses of 2 c.cm. of a 10 per cent. solution diluted with five times its volume of normal saline. The injections may be continued for several weeks at intervals of three or four days. In conjunction with the mercurial diuretics it is advantageous to give ammonium chloride by mouth (gr. 15–30, t.i.d.). When in spite of these various measures fluid continues to accumulate in the tissues and serous cavities, paracentesis of the chest and abdomen and drainage by multiple punctures in the calf of the leg may be necessary. These procedures (which must, of course, be carried out with strict aseptic precautions) are, however, to be regarded as a last resource, when all other methods of treatment have failed.

AFTER-CARE

After the venous pressure has returned to its normal level, a prolonged period of convalescence is required before the patient is capable of resuming his full activities. At this stage massage to the limbs and back is helpful in restoring tone to muscles which have become flabby owing to disuse. This should be followed by active movements and resistance exercises. When first the patient is allowed out of bed, he should be content to sit in a chair for half an hour, and his further progress must be carefully regulated in accordance with the response of the heart to exercise, as determined by attention to subjective symptoms, such as fatigue, and quickening of the pulse rate. Finally, graduated walking exercise may be started, at first on the level and later on suitable inclines. It cannot be too emphatically stated that throughout this training, the patient's activities must never exceed the limits of his tolerance.

When convalescence is complete, the future still remains to be considered. An attack of congestive heart failure must be regarded as an acute exacerbation in the course of a chronic disease. Treatment, therefore, does not end with the subsidence of the attack, for steps must be taken to prevent its recurrence. The patient must be warned against over-exertion, on the one hand, and insufficient exercise on the other. Whereas the former may precipitate a sudden attack, the latter will produce a gradual impairment of his cardiac reserve. He must steer a middle course. He must lead a quiet regular life and keep under medical supervision.

The advice which I give patients with chronic heart disease, may be summarized by saying that they must observe moderation in all things, taking regular exercise, within the limits of their tolerance, but never making any sudden effort which entails exerting their full strength, or which produces dyspnœa. For example, they must never run for a train, struggle against the wind, or attempt to start their motor car by hand. They must always stop eating before they are satisfied, and sit quietly in a chair for half an hour after meals.

In the event of any intercurrent infection, such as an attack of bronchitis, or even a common cold, they must at once take to bed. The amount of rest required during the day depends on the severity of the cardiac lesion; but, in patients whose reserve is extremely limited, one whole day in bed each week will often enable their hearts to carry on for many years in a fairly satisfactory fashion. Those who are able to resume their work must put their health before their business, for if their health breaks down, their business will go too.

ORGANIC, FUNCTIONAL AND NERVOUS FACTORS

The measure of success which may be anticipated in the treatment of a particular case of congestive heart failure depends on the extent to which the symptoms are attributable to the underlying structural lesion, on the one hand, and to derangements of the cardiac function on the other. Functional derangements are generally amenable to treatment, whereas structural changes are permanent and so determine the fixed and unsurmountable limitation of the cardiac reserve. Just as a healthy person can improve his " wind " by athletic training, so a cardiac patient can by suitable treatment increase his cardiac reserve, though he can never hope to attain to such a high level of exercise tolerance as the man with a normal heart. Conversely just as the healthy person leading a sedentary life gets " out of training " and is easily " puffed," so the patient with chronic heart disease, by failing to observe the precautions outlined above may lose ground to such an extent that ultimately he develops congestive heart failure. The cardiac reserve can always be increased by appropriate treatment, but whether it can be increased sufficiently to enable the patient to carry on, depends on the extent of the permanent structural lesion.

In addition to the structural lesion and the disturbances of function resulting from derangements of the cardiac mechanism, there is a third factor which plays a part—sometimes trivial, but often important—in modifying the clinical picture. This is the psychological element. This aspect of the subject merits special emphasis in the present connection, because its importance is not always sufficiently appreciated, and it is a complication which cries out for treatment.

In every case the element of neurosis plays some part in aggravating the patient's symptoms. The more introspective the individual, the greater will be the aggravation so produced. But quite apart from this simple psycho-neurosis, there are often other mental complications. Consider, for example, the state of mind of a man suffering from chronic heart disease, who is laid low with an acute exacerbation of heart failure, perhaps brought on by an attack of bronchitis or influenza. He realizes that his life is in the balance, and that if his illness terminates fatally he will be unable to make provision for his wife and family. Similarly in all cases of prolonged illness, it is essential to weigh carefully the physical damage which may result from allowing a patient to return to his work before convalescence is complete, against the mental trauma when he sees his business going to pieces, and the future of his dependants at stake. However competent a practitioner may be in other respects, he will fail to get the best results from treatment if he does not realize the importance of the psychological factor. The confidence of a patient in his practitioner depends on something more than mere knowledge and scientific ability, and it is that confidence which often holds the balance between success and failure.

THE TREATMENT OF AURICULAR FIBRILLATION AND FLUTTER

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THE discovery of the action of digitalis in heart disease by Withering more than 150 years ago was a clinical observation which must be reckoned a landmark in the field of medical science and practice. The chance information which he had obtained from a family recipe proved a turning point in the history of the treatment of heart failure. The experience of this acute clinician established on a secure foundation a drug which is now recognized as satisfying the exacting standards required of a specific remedy. He reveals the spirit of scientific rectitude which guided him in his investigations, when he writes in a letter to a friend concerning the use of digitalis : " It is much easier to write upon a disease than upon a remedy. The former is in the hands of nature, and a faithful observer with an eye of tolerable judgment cannot fail to delineate a likeness. The latter will ever be subject to the whims, the inaccuracies, and blunders of mankind." After ten years' experience he published his results in a memorable treatise which will always remain a milestone in the story of digitalis therapy. Although impressed by the effect of digitalis as a diuretic he realized that it had a definite action on the heart. His recommendation to give it in sufficiently large doses until it acts on the kidneys, the stomach, the pulse, or the bowels, is advice which could not be improved upon at the present time. For more than a century no progress was made in the treatment of heart disease with digitalis. The great advance in our knowledge of its use came when Mackenzie by clinical bedside observations discovered the specific action of the drug in what we now know to be auricular fibrillation. Clinical experience in the treatment of auricular fibrillation in its relation to heart failure has proved the value of his work.

The most critical moment in the history of a cardiac malady is the onset of congestive failure; the symptoms are characteristic, the clinical effect profound, and the causal mechanism is in the majority of cases closely related to a disorder of function produced by fibrillation of the auricles. With the onset of auricular fibrillation the auricles are virtually paralysed, rapid and irregular impulses are transmitted to the ventricles, and the contractions of these chambers are rapid and grossly irregular. This disordered action of the ventricles places a heavy burden on the heart muscle, and when there is underlying myocardial disease symptoms and signs of muscle weakness develop rapidly and cardiac failure is imminent in untreated cases. This disordered rhythm may occur in paroxysms lasting a few minutes, several hours, or occasionally days before the normal rhythm is restored. In the intervals between the attacks there may be no symptoms referable to the heart, and if the myocardial defect is slight the attacks do not lead to serious consequences. Infrequent and short paroxysms are not disabling and therefore do not require special treatment. They are sometimes related to an infective process, and when this has been controlled the attacks may not recur. Paroxysms of auricular fibrillation are a common complaint in young subjects with rheumatic heart disease, particularly in those with mitral stenosis; in older patients with degenerative changes in the myocardium and arteries; and in a well-defined group with thyrotoxicosis.

The main object of treatment in the attack is to make the patient comfortable until the normal rhythm is restored; reassurance as to the nature of the seizure is often required, and a sedative will help to remove a natural anxiety. A chloral hydrate mixture in 10 grain doses, repeated at four- or six-hourly intervals three or four times is useful for this purpose. Chloralamide in cachets, gr. 10, repeated in the same way is equally effective in calming the patient. An ice-bag applied to the precordium may relieve the discomfort felt in the region of the heart. Firm pressure on the carotid sinus over the carotid artery below the angle of the jaw for ten or fifteen seconds may release a mechanism, through the vagus nerve, which can terminate the attack. If vomiting is induced the paroxysm may be shortened. Quinidine sulphate gr. 3, given every four hours is the only drug known to have a specific effect in controlling this disturbance of rhythm. Digitalis should be withheld as it may establish a chronic state of fibrillation. A prolonged rest is not required after the normal rhythm has returned unless symptoms of heart failure have developed during the attack. Quinidine may be prescribed between the attacks for its effect in lengthening the intervals and shortening the duration; the dose is gr. 3 t.d.s.; if necessary it can be increased to gr. 15 in the twenty-four hours; a good practice is to prescribe the extra gr. 6 to be taken at bedtime; the patient need not be kept at rest on this dosage.

When auricular fibrillation has lasted for a longer period than ten days it will not revert to a normal rhythm spontaneously, and is a chronic malady. This rapid and irregular action of the heart when established is the chief cause of congestive failure and is always a serious condition in untreated cases. Symptoms of heart failure develop rapidly in those with advanced structural disease, such as mitral stenosis with much enlargement, hypertensive heart disease, and coronary atheroma. In others without chronic disease of the heart muscle symptoms of myocardial exhaustion may be delayed and the circulation well maintained for a long period.

The object of treatment is to relieve the heart of the heavy task which the rapid ventricular rate produced by the fibrillation has imposed on the ventricles. The slowing of the increased ventricular rate can be obtained by giving digitalis in doses which are large enough for the drug to accumulate in the tissues of the body. The usual practice is to give a drachm of the tincture daily for five days or a week, when the ventricular rate may be expected to fall to 70 or 80; at this level the dose should be halved, and continued so long as the rate does not fall below 60. Profound slowing, with coupling, nausea, vomiting and diarrhœa, as evidence of over-dosage, are indications for withdrawal of the drug and complete rest. When these toxic effects have disappeared, digitalis control can be resumed in the amount required, and given as a maintaining dose if the heart rate reaches 90 per minute at rest. Gastric symptoms may be avoided by prescribing the drug well diluted and after food. The patient should always be kept at rest when digitalis is given in large doses during the initial stages of the treatment. It is sometimes necessary to obtain a quick response and a rapid slowing of the heart by giving the drug in massive doses. The dosage in these circumstances for an adult with body-weight of 140 lbs. is 1½ to 2 drachms of the tincture in a single dose, and repeated twenty-four hours later if the rate remains high, followed by 20–30 minims daily. Massive dosing is dangerous if there is digitalis in the body at the time, and the patient cannot be kept under close observation, for the toxic effect may be rapid and produce fibrillation of the ventricles and sudden death. The daily administration of 20 minims of the tincture is a minimal maintenance dose for an adult; a smaller dose is not sufficient to control the rate, for a larger amount, averaging 20 minims is destroyed daily by the body tissues. The white Nativelle's granule digitalin gr. 1/240, is the equivalent of about 20 minims of the tincture, and is a convenient and reliable preparation. The tincture of strophanthus is sometimes prescribed when digitalis is not tolerated. The initial doses are 20–30 minims daily. Compared with digitalis it is an unsatisfactory drug and is rarely required as a substitute. Strophanthin can be given in cases of urgency. An intravenous injection of gr. 1/250 in 1 drachm of saline and repeated in two hours, produces a rapid slowing of the ventricles; it should precede and never follow digitalis administration. The dosage of digitalis or strophanthus can be determined with a considerable degree of accuracy by giving the patient the quantity that makes him most comfortable. The ventricular rate should not be lowered below 90 when there is fever, as the cumulative effects of over-dosage can occur if lower rates are maintained.

Our main objective in treating auricular fibrillation is the control of the heart rate. It is possible to obtain this object in some patients by restoring the normal rhythm with quinidine. The results are dramatic, and there is very little risk in selected cases. The most suitable for quinidine therapy are those presenting few signs of structural disease, with no enlargement of the heart and no valve disease. This drug should not be given if there is much enlargement, congestive failure, or a history of hæmoptysis. Quinidine may have to be prescribed in large doses up to 30 grains daily and continued for a week or longer before the fibrillation is replaced by a normal rhythm. Absolute rest in bed is essential, until the fibrillation is abolished or the treatment discontinued; it is desirable to keep the patient in bed for a fortnight after the normal rhythm has been restored. If the fibrillation persists after ten days of treatment the daily administration of quinidine, gr. 30, may be continued for a further period of a week or ten days, but is not likely to be effective in restoring the normal rhythm. The initial dose should be small, in case there should be any idiosyncrasy for this drug; gr. 3 the first day, gr. 6 on the second day, and on the third day gr. 6 three times daily, and afterwards gr. 30 evenly spaced over the twenty-four hours. When the rhythm has returned to normal the dose should be reduced to gr. 6 two or three times daily for a week, and afterwards gr. 12 daily for a month or longer.

Auricular flutter is a disorder of the heart's rhythm caused by the rapid and regular beating of the auricles with the rate between 260 and 320 to the minute. The ventricular rate is increased and is usually half the auricular rate, i.e. 130 to 160 per minute. Conspicuous rapid and regular heart action which is persistent and is unaffected by change of posture or exercise is a characteristic feature of this condition. When the ventricles beat rapidly and irregularly, as they may do, it is difficult to distinguish auricular flutter from auricular fibrillation without the aid of an electrocardiogram. The two conditions closely resemble one another in their causal mechanism. In both there is a disorder of rhythm caused by a circulatory wave in the auricles; in fibrillation the wave travels at a more rapid rate, and takes a more irregular course. This circus movement in the auricles is responsible for the rapid contraction of the ventricles, and the clinical effect resulting from the increased ventricular rate. In patients with auricular flutter, as in those with auricular fibrillation, a heavy load is thrown on the ventricles, and the object of treatment is to relieve the heart of this extra work by slowing the ventricular rate. This can be done by giving digitalis in sufficiently large doses to produce the required slowing of the ventricles, and by continuing the use of this drug in doses that will maintain a slow ventricular rate. This remedy has a specific action in flutter as in fibrillation, and in the general management of the cases the rules governing its administration are the same. The initial doses are heavy, a drachm a day of the tincture for a week, followed by a daily maintenance dose of 20–30 minims. When the rate of the ventricles has reached 70 or 60, the heart may become grossly irregular with the onset of auricular fibrillation, and if the drug is discontinued at this stage the fibrillation may be of short duration and the normal rhythm permanently restored. In the majority of treated cases chronic fibrillation is established and the ventricular rate can be controlled by resuming treatment with digitalis. In some, if the patient is kept digitalized, the flutter persists, a high grade of auriculo-ventricular block is produced, and the ventricles beat at a slow rate, and heart failure can be arrested.

Quinidine can be employed with the object of restoring the normal rhythm, and is sometimes successful, but in most cases is an unsatisfactory remedy. The dosage and the management of the case is that of auricular fibrillation.

Paroxysmal flutter is rare as compared with paroxysmal fibrillation, but the treatment is the same and need not be described.

Auricular fibrillation is a disorder of rhythm frequently observed in thyrotoxic subjects. The treatment is that of toxic goitre. A normal rhythm returns after a thyroidectomy in about half of the cases so treated. If after the operation fibrillation persists, a normal rhythm can be restored with quinidine. Treatment with quinidine before the operation is rarely successful. Digitalis should be given before operation if the ventricular rate is high, and congestive failure imminent. It is only in exceptional circumstances and when the patient is moribund that auricular fibrillation contra-indicates thyroidectomy.

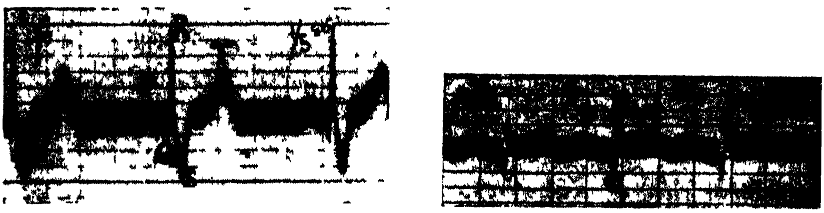
THE ELEMENTS OF ELECTRO-CARDIOGRAPHY

By CLAUDE WILSON, M.D., F.R.C.P.

ELECTROCARDIOGRAPHY, known in physiological laboratories some forty years ago, is clinically perhaps twenty years old. Though an immense amount of work has been done by an ever-increasing proportion of the profession, and though results which are final and permanent have been achieved, both with regard to the arrhythmias and to myocardial disease, the subject may still be said to be in its infancy. Ideas as to the prognostic significance of certain well-defined records have changed a good deal since the early days, indeed are still changing, and atypical records may be differently interpreted. But the elements of the electrocardiogram are agreed upon by workers in all parts of the world, and it is with the elements alone that this paper deals. Those with a firm grip of these simple premises will easily recognize a normal electrocardiogram and a good many of the more important anomalies. With this knowledge the subject can hardly fail to prove of interest, and there are ample sources for pursuing the study. No report on a heart case is now regarded as complete without an electrocardiogram, any more than a dental report is complete without X-ray chart of the teeth. In either case the information thus obtained, if normal, is valuable, and may supply the only definite evidence of disease.

Most members of the profession can follow a dental report and confirm or question the conclusions of the radiographer; but the electrocardiogram remains, up to now, a thing to be interpreted by a specialist; and many doctors will frankly confess that they know nothing about it, and that what they read in books or papers presupposes elementary knowledge which they do not possess and do not know where to find, without tackling treatises involving much close study.

A note upon a heart case may be accompanied by a short record from one of the leads of the electrocardiograph. Fig. 1 (A and B) are examples, and they convey



A B

FIG 1.—A From lead I—except for the widened S wave typically normal. B. From lead III—an emotional tachycardia—frequency 100. The sympathetic dominating the vagus.

much information to the initiated. Yet there are those who may ask: "What do the figures in the corner stand for? What do the letters mean? How is the thing produced? And what is the good of it?" It is to those only who may ask one or more of these questions that this paper and the answers are addressed: the figures stand for the leads, P represents the auricular systole, and Q R S T the ventricular.

The *electrocardiograph.*—The contraction of a muscle fibre is always accompanied by changes of electrical potential which can be converted into electric currents and recorded by means of a galvanometer if sufficiently sensitive. The heart consists of a vast conglomeration of muscle fibres arranged in a very definite manner, a single system embracing the two auricles, another system embracing the two ventricles, and a conducting mechanism uniting the two.

Leads formerly were, and in exceptional cases still are, taken from points on the surface of the thorax, but the discovery by Einthoven, the inventor of the string-galvanometer, that leads from the limbs are in every way adequate, has led to the universal practice of taking three records which supplement and complement one another, and which are transverse, diagonal, and vertical in relation to the body; while lead II corresponds roughly to the normal axis of the heart.

Lead I is taken from the R. arm and the L. arm.
„ II „ „ „ R. „ „ L. leg.
„ III „ „ „ L. „ „ L. leg.

Suitable electrodes (immersion or metallic) convey the current to the instrument. Until a few years ago the standard fixed electrocardiograph, with its Einthoven string, occupying the space of a camp-bed and preferably mounted on a concrete foundation, was the only instrument available.

Within the last few years portable instruments have appeared and, as there are four or five varieties now on the market in England, it cannot be long before the practitioner will be as easily able to obtain an electrocardiogram of a heart case as a radiogram of a fracture or a barium meal.

The instrument with which the records illustrating this paper have been taken is the "Matthews portable electrocardiograph." It is a British invention, much less sensitive to mechanical vibration than is the Einthoven fibre, and, though heavier, not much larger to carry about than a good-sized week-end suitcase. Other portable instruments possess special features which appeal to those who get accustomed to them. All electrocardiographs are intricate pieces of mechanism, and there is not room here to attempt even an elementary description of the principles upon which their beautiful results depend.

The *electrocardiogram* is the actual graphic record of the electrical changes which are being constantly evolved by the beating heart. It records physiological and pathological conditions and is a direct record of vital activity. Electrograms from all three leads are invariably taken, and are mounted one above the other, though a short extract from one lead may often be sufficient to illustrate a note upon a case.

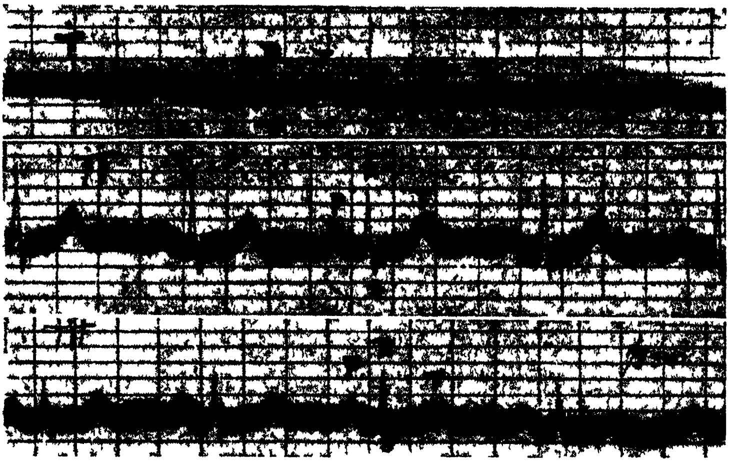


FIG 2 is an electrocardiogram taken from a normal heart and showing each of the three "grams" mounted on a background of horizontal and vertical lines

The *background* is an important element; backgrounds differ widely according to the requirements of different investigators, some being so minutely subdivided as to become confusing. For ordinary purposes a simple background, such as is here employed, suffices. The thicker horizontal lines are one centimetre apart, and the thinner ones represent decimal points. The lines are used to measure the *amplitude* or *voltage* of the excursions above and below the abscissa of the gram; and if the instrument is properly adjusted the centimetre is equivalent to one millivolt of current. Roughly speaking, ventricular excursions of more than one and a-half centimetres approach what is termed *high voltage*, while those of half a millimetre or less are said to be of *low voltage*. Fig. 2 shows good voltage in lead II, low voltage in III, and exceptionally low in I. Taking the three leads together the voltage is within normal limits. But the significance of high and low voltage is as yet imperfectly understood. Certainly the voltage of the three leads differs widely in normal electrocardiograms.

The vertical lines on the background record the *timing*, and in the records here shown they are invariably one-fifth of a second apart. The instrument is so arranged that they can be brought nearer together or spread out; but in all adjustments the timing lines are the same—i.e. one-fifth of a second.

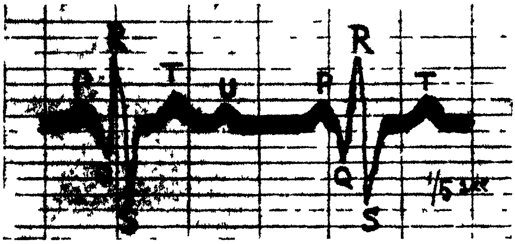


FIG. 3 is a diagrammatic representation of a single heart-beat from one lead showing *all* the points which are ever seen in a normal gram. They are labelled P Q R S T, letters chosen thirty years ago by Einthoven, as convenient and unappropriated in medical nomenclature. The U wave is of more recent origin, is very seldom seen, and, although it is important to realize that an undulation following the T wave is not necessarily abnormal, it will be ignored in this paper and P Q R S T regarded as the complete cardiogram. But in no record will all the waves be found in all the leads. Fig 2 shows all the waves, except Q, in leads II and III, while Fig. 1B shows a marked Q (lead III.)

The auricular systole.—P represents the auricular systole (Figs. 1 and 2); normally it is a peak and not a dip, and is definitely within one-fifth of a second of the commencement of the ventricular complex. It is almost invariably of low voltage, and may not be obvious in all leads or in every beat, but if it is found regularly, even in one lead, it means that the auricles are beating and are presumably healthy. Inversion of the P wave may precede an extra (premature) systole; definite notching of P suggests mitral stenosis, while complete absence of a P wave in all the leads means that the auricles are not contracting. The ventricular beats will then be found to be irregular in sequence, and in one or more leads the characteristic oscillations of auricular fibrillation will probably be seen (Fig. 4), though complete absence of P, accompanied by an irregular ventricular beat, is evidence enough (Fig. 5), for visible fibrillation is not always present.

FIG 4

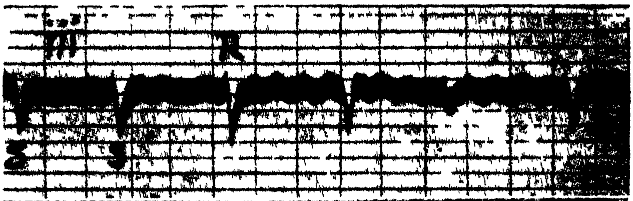
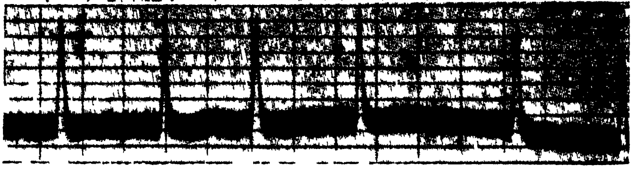


FIG.



The ventricular systole.—The Q R S complex represents the commencement of the ventricular systole (Figs. 1 and 2), and T its termination. Then from T to the following P the heart is at rest. The Q R S complex never normally occupies more than one-tenth of a second, and T follows more leisurely.

Q is a variable wave—often absent or discernible only as a trace in one of the leads, though occasionally very obvious, as in Fig. 1B. It is a sharp, short wave always pointing downwards. Its presence or absence is probably of negligible significance. R is a sharp peak pointing upwards and showing extreme varieties of voltage, while S is a sharp dip, the precise reverse of R. One or other or both of these waves is present in every beat in every lead. The left ventricle is the predominant element of R in lead I and of S in lead III. The right ventricle is the obverse, i.e. S in lead I and R in lead III. The gram of lead II is generally recognizable as the common denominator of leads I and III, and is often, though not always, the most informative of the three leads.

In lead III the Q R S complex occasionally has, in quite normal hearts, what is called a *bizarre* appearance, generally of low voltage, in which it may not be possible to label the individual points, beyond calling the whole thing " Q R S *bizarre* " (Fig. 6). If the other leads are normal, this may be ignored.

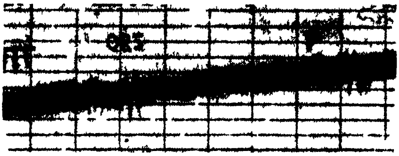


FIG 6

The T wave is of great importance in relation to the diagnosis of myocardial disease. It has a considerable variation in voltage, but it normally points upwards in leads I and II, while it may point either upwards or downwards in lead III. A flattening of the T wave is generally of somewhat sinister significance, while a definitely reversed T, dipping downwards in leads I or II, or both, though possibly of toxic origin, more generally indicates myocardial disease or degeneration. The thick abscissa which joins the various elements of the electrocardiogram is normally fairly horizontal, though many errors of the artefact variety (*see* below) may cause ups and downs, while in recent cases of coronary thrombosis there are very characteristic deviations, especially between the R and T waves, but this diagnostic complex is not within the range of an elementary disquisition. Normally the abscissa before and after the Q R S complex should be practically level on what is called the "isoelectric line." A gram such as shown in Fig. 7 suggests myocardial disease.

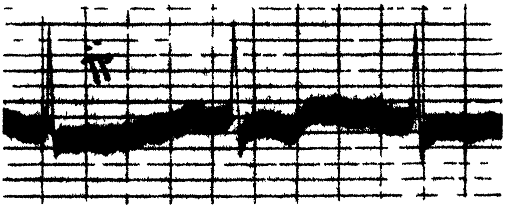


FIG. 7.

P Q R S T or P R T or P S T are, then, the elements of the electrocardiogram. But Q may be absent in all the leads, so that R or S, one or both, may be the only elements present in every beat of every lead, for P and T may both be so flattened in one, or even in two, leads that they are barely recognizable. If, however, P R T or P S T can be made out and found to be normally placed in any one lead (as in lead II, Fig. 2) it is proof that both auricles and ventricles are working normally.

P Q R S T, some or all, in endless succession, form the electrocardiogram record. Though hundreds of grams are taken every day, most of which prove to be normal, yet one may say that no two are exactly alike, any more than finger-prints. If matters were quite so simple as has up to now been suggested, the reading of an electrocardiogram ought to be a very easy task. But it is often otherwise, for, apart from the arrhythmias, which will be alluded to later, differences of voltage, of frequency, and recognized ups and downs of the abscissa, one may have to deal with what are called artefacts, abnormalities of the record arising from various causes, but not attributable to the heart-beat. If the patient coughs or moves a finger an artefact will be produced which may suggest an extra-systole; the same if the operator accidentally touches the instrument. Faulty electrodes and the lighting currents in a house, if imperfectly insulated, are frequent offenders. Thunderstorms may cause them.

The reader of books upon the heart, and of articles illustrated by electrocardiograms, will very seldom come across an "artefact." They are carefully eliminated and a fresh record is taken. Yet to the novice they are painfully familiar and must have puzzled many tyros.

In the normal electrocardiogram the waves P R S T occur at regular intervals and in regular sequence, though emotional influences may alter the frequency. But whether the heart is a slow beater (say 60) or a fast one (say 100), the timing of the events should be

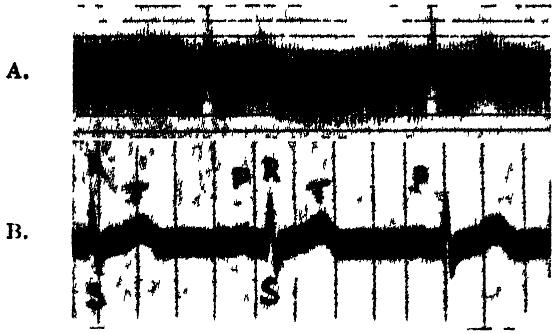


Fig. 8 gives two records. A before, B after the current was turned off at the main

perfectly regular, and two of these are of prime importance. P should not be separated from the Q R S complex by more than one-fifth of a second at the outside, and Q R S (one or all) should not occupy more than one-tenth of a second. These timings can be very easily read on a background divided into fifths of a second, though a pair of compasses should always be at hand. If the P R interval is more than one-fifth of a second it means delay in the conducting mechanism, probably in the main "bundle" (of His) before it divides, and we are dealing with a minor stage of heart-block. If the Q R S complex occupies more than one-tenth of a second the integrity of the ventricular muscle is suspect, as is also the case if the complex is notched (Fig. 9A) or truncated (Fig. 9B), a definitely abnormal gram.

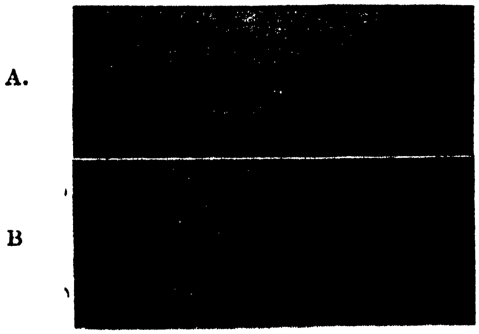


Fig. 9.

The arrhythmias.—Though very different views have been expressed regarding the value of the electrocardiogram, it is universally recognized that arrhythmias can always be thus differentiated much more easily and certainly than by any other method. Auricular fibrillation has already been described and illustrated (Figs. 4 and 5). Here there are no P waves. In auricular flutter two or even three P waves are discernible between each pair of ventricular beats. In sinus arrhythmia, so common in youth, the obvious irregularity of the ventricular systoles will be found, on scrutiny, to be accompanied by a similar irregularity of the auricles, P waves preceding Q R S at the normal distance. The irregularity arises in each beat at the sino-auricular node, and proceeds normally through the auricles to gather at the auriculo-ventricular node, and be conducted by the main *bundle* through the junctional tissues to its point of division to activate each ventricle separately, though simultaneously. Each beat is perfectly normal, but imbalance between the vagus and sympathetic causes an irregularity of time-sequence.

In heart-block there is damage somewhere in the conducting system, and if in the main *bundle* the P R interval is increased, as in Fig. 10, where the interval approaches two-fifths of a second, but sometimes to the extent of complete ventricular beats being missed. The varieties of irregularity due to heart-block are numerous, and all can be distinguished on the electrocardiogram as well as the characteristic gram of bundle-branch block, in which there is block in one

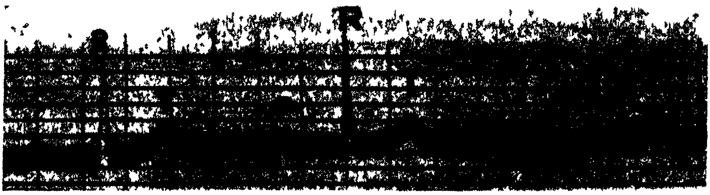


FIG. 10.

of the divisions of the bundle after it divides (Fig. 11).

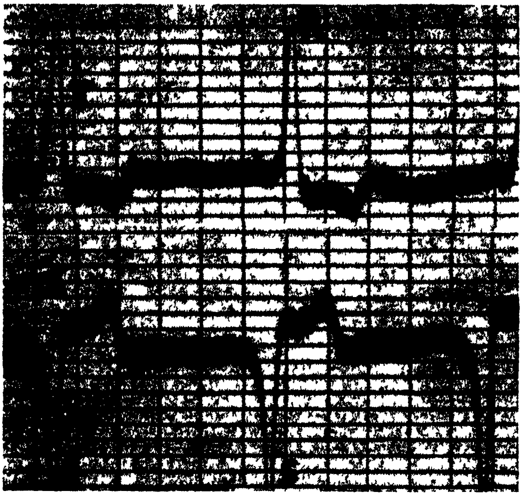


FIG. 11.—(Right bundle branch block, left ventricular preponderance.) In this case it is the right bundle branch which is blocked, giving free play to the preponderance of the left ventricle (R in lead I and S in lead III).

I have left to the end the premature beats or extrasystoles which may start in the auricles, in either of the ventricles, or in the junctional tissues, in which case the gram may be difficult to read, for the auricular beat may be simultaneous with that of the ventricles, or may even come after it. But extrasystoles originating in the auricles, or in either ventricle, are easily distinguished.

Fig. 12 shows a slow sinus arrhythmia in an old man, and one extrasystole originating in the auricle (T and P being merged). The dark colour of the whole gram is due to light having entered the dark room during development.

FIG. 12

Fig. 13, from lead III, shows two extrasystoles in sequence, X (L V) arising in the left ventricle and X (R V) arising in the right ventricle. If this gram had been taken from lead I the sequence would have been reversed, for in lead I, S represents the right ventricle and R the left.

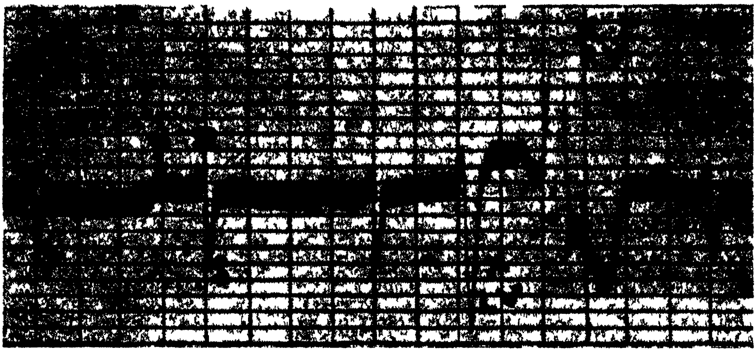


FIG. 13

The evaluation of the electrocardiogram.—It is well known that a normal electrocardiogram is not proof positive of a normal heart, and Sir James Mackenzie's aphorism: "On no single symptom or sign shall any heart be condemned," applies here as elsewhere in cardiology. Bundle-branch block, for instance, has been shown by statistics to have a serious prognostic significance, but it is now known that there is a congenital variety consistent with longevity and good health. The subject from which Fig. 11 was taken (æt. 70) is known to have shown a similar electrocardiogram ten years ago, and has not had any cardiac symptoms. Still, obviously damaged hearts generally give abnormal electrocardiograms, whereas apparently healthy ones but seldom do. There remain the difficult cases in which doubt exists after clinical investigation of the heart. Here a normal electrocardiogram is very reassuring, whereas an abnormal one (with, say, inverted T waves in leads I and II) arouses serious warning. I append a few cases illustrating the value of the electrocardiogram in clearing up conditions otherwise unrecognizable.

Case 1.—Auricular fibrillation can be recognized clinically in nineteen cases out of twenty, but occasionally a shower of extrasystoles or a mixture of sinus arrhythmia with extrasystoles is diagnosed as fibrillation, and a gram shows that the diagnosis is wrong. Similarly, I have lately seen a case in which I diagnosed extrasystoles with normal rhythm, but where the electrocardiogram showed auricular fibrillation. Full digitalization dissipated the symptoms.

Case 2.—An elderly gentleman complained that once or twice, while playing bridge, he had slipped off his chair and was momentarily unconscious. "Was it his heart?" he said. Clinically I could find nothing wrong, and I thought it was a case of petit mal. A gram however, showed a much prolonged P R interval (Fig. 10), and I have no doubt that his attacks were due to the missed beats of heart-block.

Case 3.—A lady walked from her hotel to my house and arrived very breathless and cyanosed. Her pulse was regular at about 80, the heart did not appear to be enlarged, and the sounds were normal. After a week in bed the clinical signs were the same, but all symptoms had vanished. Fortunately, I had taken an electrocardiogram at her first visit, and I took another later. The first showed auricular flutter, the second was normal.

Case 4.—The patient (a practitioner in the sixties) complained of having on one occasion felt "weak and cold" and found his pulse beating very slowly. Physical examination passed his heart as sound, but the electrocardiogram (Fig. 9B), was obviously abnormal. Two months later he had an attack of complete heart-block (Stokes-Adams syndrome).

It is needless to cite more examples. Everyone who works with an electrocardiograph among clinical cases comes across similar instances, though perhaps the happiest and most frequent help afforded lies among the many cases in which more or less vague symptoms have been diagnosed by someone as of cardiac origin, but where the physician with specialized experience has his doubts, which, if supported by a normal electrocardiogram, carries conviction to all concerned, and releases the patient from needless restrictions and paralysing fears.

PRACTICAL NOTES

Toxic Goitre and its Treatment

The January number of the *Australian and New Zealand Journal of Surgery* is a "Melbourne Hospital Number" and contains an important article on toxic goitre (1933, ii, 244) by H. Hume Turnbull and Alan Newton, who are respectively in charge of corresponding medical and surgical wards in the hospital, with a note on pathology by Peter MacCallum, professor of pathology at Melbourne University. The cases studied consist of a series of 348 consecutive cases of toxic goitre treated by thyroidectomy during the past eight years by Newton, an additional 175 cases in which the toxic signs were slight or absent being excluded. The authors divide toxic goitre into (*a*) exophthalmic goitre, (*b*) nodular toxic goitre, with and without antecedent acute signs, and (*c*) the toxic single lump. The experience gained from this series of cases confirms the belief that it has become a very common practice to treat patients suffering from toxic goitre with iodine for long periods in the hope of effecting a cure. The majority of these patients are eventually advised to undergo surgical treatment which is rendered much more difficult by the previous iodine therapy. It has been conclusively demonstrated by many observers that iodine, though it commonly produces a complete remission when first administered, will not maintain this state indefinitely, and that a toxic condition, often more severe than that originally present, recurs. In the present state of our knowledge, it seems reasonable to insist that iodine should not be used in the medical treatment of thyrotoxicosis, but should be confined to pre-operative preparation. Many writers on this subject insist that focal infections should be sought for and removed before thyroidectomy is performed, but the basis for this advice seems to be unsound. The evidence brought forward to show that hyperthyroidism is due to the effect of poisoning from infection in some other organ is unconvincing, and there is a conspicuous absence, in the literature, of reports of cases in which, though the condition was sufficiently severe to make operation reasonably probable, patients have been saved this necessity by the removal of focal sepsis. A preliminary operation for removal of the tonsils, for example, is a very severe trial for a patient suffering from hyperthyroidism, and, further, if the risks of this procedure are reduced by the administration of iodine, the remission will be over before the patient is ready for thyroidectomy, the risk of this operation being thus greatly increased. Plummer and Charles Mayo, junr. state that though, in their experience, patients with exophthalmic goitre are prone to have tonsils from which fluid pus can be expressed, it is their impression that the tendency to attacks of acute tonsillitis, which seems to exist in cases of this nature, usually has developed after, rather than before, the onset of the exophthalmic goitre. In all cases of toxic goitre the first operation performed should be thyroidectomy. If focal sepsis be present and if it continues to give symptoms, it can be treated more safely and more easily after recovery from the thyrotoxic symptoms. It is interesting to note that Joll, in a review of 795 cases of toxic goitre, expresses a similar opinion. No statement of the work done in Melbourne on toxic goitre would be complete without acknowledgment of the valuable work previously done there by T. P. Dunhill. Owing largely to his influence, the authors state, the great majority of medical practitioners advise, and their patients willingly and cheerfully undergo, operative treatment for this disease. The modern operation for toxic goitre is a bilateral resection of the thyroid gland, leaving only a small bit over the recurrent laryngeal nerve on each side. The gradual evolution of this operation in the last three decades is due to the work of many distinguished surgeons in different countries, but it is not yet universally recognized that Dunhill was the first to stress the importance of an extensive bilateral resection of the gland in this disease. There is still some difference of opinion concerning the advisability of performing this resection in one stage. In the earlier cases in this series a two-stage removal of the gland was the routine procedure, but, as a "follow-up" investigation of these patients revealed certain disadvantages of the method and, perhaps, as surgical confidence increased with experience, it was replaced by a bilateral one-stage removal.

The Treatment of Rheumatoid Arthritis

Russell L. Cecil discusses recent developments in the field of arthritis, and shows how this newer knowledge can be applied in the diagnosis, prognosis and treatment of joint diseases in general and of rheumatoid arthritis in particular (*Journal of the American Medical Association*, April 22, 1933, c, 1220). The majority of cases of chronic arthritis fall into one or other of two great groups. Rheumatoid arthritis is a clearly defined clinical entity which in most cases can be accurately differentiated from osteoarthritis and from the so-called specific forms of infectious arthritis. Rheumatoid arthritis has its own pathology and usually runs a characteristic clinical course. Hypertrophic arthritis, on the other hand, appears to be a degenerative, senescent process. Evidence is rapidly accumulating that rheumatoid arthritis (like rheumatic fever) is a chronic infection. This evidence comes from pathological, bacteriological, serological and clinical sources. Allergy probably exerts an influence on the disease, but no more than in other chronic infections. In rheumatoid arthritis a primary focus of infection is the portal of entry for the exciting agent. In respect to its pathogenesis, the author considers the disease analogous to gonococcal arthritis, which it often resembles closely. The foci and the infectious agents are different, the mechanism of infection the same. By employing new bacteriological methods, a number of investigators have succeeded in cultivating streptococci from the blood and joints of patients with rheumatoid arthritis. While these observations have not been confirmed in some laboratories, the presence of specific streptococcal agglutinins in the serum of rheumatoid patients would seem to refute the theory that these micro-organisms are contaminations.

Furthermore, the ease with which an experimental arthritis can be produced in rabbits by intravenous injection of these streptococci lends strong support to the proposition that rheumatoid arthritis is a streptococcal infection. The specific streptococcal agglutinins that are found in the serum of a high percentage of patients with rheumatoid arthritis are of considerable value in differentiating rheumatoid arthritis from other forms of chronic arthritis. The sedimentation rate is useful in separating rheumatoid arthritis and the other infectious forms from non-infectious ailments of the joints. By making use of the agglutination and sedimentation tests and the Schilling count, the practitioner is now in a position not only to make a more accurate classification of arthritic patients, but also, by repeating the tests from time to time, to gauge the activity of the disease and the efficacy of the treatment. The rational treatment of rheumatoid arthritis embraces removal of foci of infection, emphasis on rest, and a general building-up programme, consisting of carefully regulated diet, vitamins, iron and arsenic, and adequate elimination through the intestine, bladder and skin. Streptococcus vaccine, administered intravenously, is of considerable value in many cases, though its *modus operandi* is not yet understood. Physical therapy, if carefully supervised, is useful in stimulating the local and general circulation. In advanced cases, orthopædic surgery may solve an otherwise baffling problem.

X-ray Examination of the Nasal Accessory Sinuses in Infants and Children

The frequency of infections of the nasal accessory sinuses in adults is admitted by all rhinologists and radiologists; the medical profession has not accorded the same consideration to children. All children with chronic coughs should, says Frederick K. Herpel (*Radiology*, March, 1933, xx, 183), have an X-ray examination of the nasal accessory sinuses. Before tonsillectomy is resorted to, sinus examinations should be frequently made. In the presence of an otitis media and mastoiditis, it is often advisable to make a sinus X-ray examination, as the sinuses will not infrequently be found affected as well. Chronic sinus infections may be followed by chronic bronchitis and bronchiectasis. The sinuses are seldom suspected in the coughs of children, and all too frequently the child is given a course of tonics and cough mixtures without avail, when the cause of the cough lies in a sinus infection. Many of these patients are afebrile, and clinically appear in quite good health, aside from the distressing cough. Swimming, and especially diving, appear to lead quite frequently to sinus infections. The common finding in sinusitis of infants and young children is a clouding of the ethmoid cells, and of one, or both, maxillary sinuses. It is probable that the ethmoid infection is primary. Thickening of the trabecular walls is noted in the chronic ethmoid infections. After clearing of the pus from the sinuses, one may note, particularly in the maxillary and sphenoid sinuses, thickening due to hyperplastic changes in the lining membrane. Osteomas may be noted in quite early childhood. Polypi are shown in the maxillary sinuses as circumscribed densities, uniform in shadow density, projecting into the antral cavity. Large polypi in the ethmoid cells may cause a broadening of the ethmoid cell area, and a thinning of the trabeculæ. Clearing of a sinus infection may be shown just as definitely by roentgenographic as by clinical examination. The author does not believe that the use of opaque oils in sinus examination is either necessary or advisable in children. The rapid improvement noted in many of these children under conservative treatment of the sinus infection makes it highly advisable that we recognize early sinus infections in children, before the secondary chest affection has become established. Early recognition and promptly instituted conservative treatment offer the best method of combating these chronic sinus and chest conditions.

The Treatment of Migraine

H. Baillard insists (*Journal des praticiens*, April 29, xlvii, 1933, 281) that migraine is usually caused by digestive disturbances, and that the best method of treatment is by dieting, combined with daily doses of calomel. The diet should be chiefly vegetarian, with the addition every two or three days of fish, chicken, a lamb cutlet or an egg. In one patient one kind of meat but not another is well tolerated, and even different methods of cooking an egg suit one patient rather than another. According to the author, the best way of giving calomel is to give it daily for ten or fourteen days in ⅛ to ½ grain doses. Aloes in small doses is also useful for migraine, especially when constipation is present; it is quite a mistake that the continued taking of aloes in small doses causes hæmorrhoids. The author has not found peptone, as recommended by Pagniez, to be efficacious. But in obstinate cases spa treatment is often successful.

The Treatment of Diarrhœa and Vomiting in Infants

J. Bruce Young has published a practical article on the treatment of diarrhœa and vomiting in infants (*Lancet*, April 1, 1933, i, 677), derived largely from his experience in London poor law institutions. The author has come to place great reliance upon gastric lavage and intra-peritoneal salines. The drugs ordinarily used (such as bismuth, calomel in small doses) are of little service in severe diarrhœa, and in his experience there is one remedy which is of value, namely, kaolin, but large amounts must be given in severe infantile diarrhœa. Kaolin can be given by the mouth, but as in the case of water given by the mouth the infant can seldom take as much as it needs. This difficulty can be overcome by administering large doses of kaolin directly into the stomach through the œsophageal tube and funnel. Splinting the infant's arms to avoid the possibility of auto-reinfection is considered to be an important point in treatment. In view of the frequency of parenteral infections, the prognosis of infantile diarrhœa and vomiting still remains guarded. Nevertheless, all things considered, the treatment outlined by the author gives good results. Good nursing is all important in promoting recovery.

REVIEWS OF BOOKS

Diseases of the Heart: Described for Practitioners and Students. By SIR THOMAS LEWIS, C.B.E., F.R.S., D.Sc., M.D. London: Macmillan and Co., 1933. Pp. xx and 297. Figs. 45. Price 12*s.* 6*d.*

THIS is a remarkable book not only on account of the authority of the author's experience in research and teaching, but for its masterly simplicity and conciseness in presenting what every man in practice should know. It represents what Sir Thomas Lewis has seen and proved, not what others have thought or written, and there is a refreshing freedom from discussions of the divergent opinions of other workers. Emphasis is laid on the importance of looking at cardiac disease from the aspect of functional disturbance rather than from an anatomical point of view, and the thirty chapters dealing with the more common disorders of the cardio-vascular system are arranged on these lines. Beginning with cardiac failure and its manifestations, breathlessness, venous congestion and œdema, the author then describes coronary thrombosis and angina pectoris; in connection with the unfortunate term "angina pectoris vasomotoria" it is pointed out that the condition is so rare that no cases of precisely the same kind have been described since 1867; the symptoms resemble those which may follow the intravenous injection of adrenaline and suggest that vaso-constriction, by throwing a considerable burden on a weak heart, which is free from disease though not necessarily wholly efficient, can bring about considerable thoracic distress or actual angina. In the account of minor irregularities of the pulse, which were formerly all regarded as of grave significance, the normal sinus arrhythmia of childhood is given as one of the numerous examples in clinical medicine of how seriously signs may be misinterpreted until they are properly investigated. Of the forms of syncope vaso-vagal and postural fainting are common, whereas cardiac syncope properly so called, which may be due to the ventricles beating slowly or very rapidly, 250 or more, is rare. After a clear criticism of the meaning of the term "compensation" Sir Thomas concludes that the diagnosis of venous congestion is within the reach of all, as it is a simple expression of what is visible, but "the diagnosis of 'broken compensation,' in its proper sense, is within the reach of none." The term "physiological syndrome of effort" is employed for the symptoms and signs brought out by strenuous exercise in a healthy person, and "effort syndrome" for the same manifestations in persons, especially the young, who are not in good health and may have some infection. The chapter on essential hypertension is packed with wise advice, and, like the rest of this thoroughly practical guide, should be read by every medical practitioner.

The Professions. By A. M. CARR-SAUNDERS and P. A. WILSON. Oxford: at the Clarendon Press, 1933. Pp. viii and 536. Price 25*s.*

THIS is a most comprehensive study of the history and development of professional association and of the related social, economic and ethical problems, which has never before been treated on the same broad lines. A distinction is drawn between professions, such as the law and medicine, on the one hand, and vocations, such as the mercantile marine, stockbrokers and produce brokers, on the other hand. The Church is omitted because its functions are spiritual, and the Army because the services which soldiers are trained to render are of a nature which it is hoped they will never be called upon to perform. The medical profession is considered very fully and on the whole with sound insight and fairness. Especially is this the case with regard to unqualified practitioners who, being free from restrictions as to advertising, have a financial advantage, and who fall into two groups, the quacks who are as unfitted to treat as they are to diagnose, and those who, though skilful in some specialized form of treatment, are not capable of forming a diagnosis; the authors definitely state that there was not any substance in the demand that Sir Herbert Barker should be recognized as a doctor and given a medical degree. The British Medical Association and the General Medical Council receive full attention; the activities of the Association in connection with the National Health Insurance Act, 1911, and the importance of the *British Medical Journal* in medical science are dwelt on; the General Medical Council's action in connection with the Axham case and the " warning notice " about " covering " are independently discussed. It is interesting to hear that it took the General Medical Council twenty years from its establishment in 1858 to get into its stride, and that at first the ancient corporations were in no mood to listen to the admonitions of this upstart body, and for some years snubbed and flouted it with impunity; but about 1886 the Council asserted itself and since then its prestige and authority have steadily increased.

The Anatomy of the Eye and Orbit. By EUGENE WOLFF, M.B., B.S., F.R.C.S. London: H. K. Lewis & Co., Ltd., 1933. Pp. 303, illustrations 173. Price 31*s*. 6*d*.

THE author is an ophthalmic surgeon, a pathologist and a lecturer in anatomy, and this book is the product of his labour and experiences in these three fields. It contains descriptions of the bony orbit and accessory nasal sinuses; the histology of the eyeball; the appendages of the eye; the anatomy of the muscles, nerves, and blood supply of the eye and orbit; the optic nerve and its central connections; the involuntary nervous system and the path of the light reflex. There are chapters devoted to the normal appearances of the human eye as seen with the slit-lamp and corneal microscope; to the development of the eye; and comparative anatomy. The author has animated his anatomical descriptions with allusions to those features of applied anatomy which are of clinical, pathological and surgical interest. The illustrations are excellent throughout the book, particularly the drawings of the author's dissections, where the craft of both the dissector and the artist are shown to good advantage. Some of the diagrams have been borrowed from Salzmann's "Histology of the Eye," from Quain's

"Anatomy" and other sources. A comprehensive bibliography is given at the end of each chapter. The paper, print and reproduction are admirable and this book is of much interest to ophthalmic surgeons, practitioners and anatomists.

Food and the Principles of Dietetics. By ROBERT HUTCHISON, M.D., F.R.C.P., and V. H. MOTTRAM, M.A. Seventh Edition. London: Edward Arnold & Co., 1933. Pp. xvi and 630. Coloured plates 3, figs. 33. Price 21*s.*

Since the first edition appeared in 1900 this work has commanded the confidence of the medical profession, and now appears with Professor V. H. Mottram as joint author. During this century it has continued to present a sound summary of existing knowledge, and in spite of all the additional data accumulated during this period, the present volume is only about eighty pages longer than the first edition. This is a tribute to constant judicious revision, for most authors experience considerable difficulty in sacrificing what they have once printed. In an admirable summary of vitamins in the first chapter it is pointed out that there is very little evidence that Vitamin E, the presence of which in the diet of albino rats is essential for reproduction, is deficient in human diets, or indeed that the above results apply to man, as witness the fertility of the poor whose diet contains very little of this vitamin. A warning about dogmatism in connection with diet sheets is wisely thrown out, for each person is a law unto himself, and idiosyncrasies depend on the endocrine and nervous make-up of the individual. The principles of diet in infancy, health and disease are set forth and illustrated with a wealth of information, references, and of that rare but invaluable property sound common sense. We should also be grateful and hug the compliment at the end of the chapter on overfeeding and underfeeding to the effect that "the proverbial good nature of the Englishman may, perhaps, be associated with the fact that, as a rule, he is full fed." The question of the amount of protein to be given in the various forms of renal disease is most successfully discussed, and it is shown that if there is too little protein in the diet of chronic nephritis, cardiac compensation may break down and uræmia result, and that for this reason an exclusively milk diet is not suitable for this form of kidney disease. In the interesting account of some dietetic "cures" and "systems" it is suggested that as vegetarianism, the purine-free diet, Hare's system, and, to some extent, the "exclusive protein diet" are all recommended by their advocates for much the same disorders, the explanation of this apparent paradox is a common factor in these opposite systems and that this may be a more complete oxidation of the proteins.

Vitamins and other Dietary Essentials. By W. R. AYKROYD, M.D. London: William Heinemann (Medical Books), Ltd., 1933. Pp. 218. Price 7*s.* 6*d.*

BRIGHTLY written and easily read, this account of the vitamins A, B, C and D, or accessory food factors, and the deficiency diseases due to their absence leads up to the closely allied subjects of scientific dietetics, the dietary value of food-stuffs, the factors which govern the dietary habits of mankind, the relations of nutrition, physique and health to food, and lastly a discussion of the perfect diet. As an example of the picturesque way in which points are brought out, reference may be made to the comparison of an elderly woman with osteomalacia, her body doubled up and supported on two sticks and her face twisted by pain into an appearance of malignancy, to the pictures of the medieval witch. The object of this book, namely, to interest the general reader, and also scientific workers and medical practitioners whose activities are chiefly in directions other than dietetics, should be successful.

A Standard Classified Nomenclature of Disease compiled by the National Conference on Nomenclature of Disease, edited by H. B. LOGIE, M.D., New York. The Commonwealth Fund. London: H. K. Lewis and Co., 1933. Pp. xvii and 701. Price 21*s*.

THOUGH the nomenclature and classification of disease are constantly altering, uniformity for the time being is important for the purposes of registration and public health statistics and comparison. In the United States of North America there have been many different nomenclatures, and accordingly five years ago a conference was held at the invitation of the New York Academy of Medicine for the purpose of remedying the existing confusion. This full and carefully thought out volume is the result of much work and consultation with various interested societies, hospitals and government departments. It is intended to include every disease which can be recognized clinically, employs English terms whenever possible in preference to Latin or Greek names, and the system of classification is based on both topographical and etiological considerations.

The Nervous Child at School. By HECTOR CAMERON, M.D., F.R.C.P. Oxford Medical Publications. London: Humphrey Milford, 1933. Pp. vii and 160. Price 6*s*.

BEFORE the war there were two London physicians, Drs. Leonard Guthrie and F. E. Batten, much interested in the psychological and nervous affections of children; since the war psychology has greatly advanced and deservedly come much more into ordinary medical practice. Dr. Cameron, who some years ago showed this in connection with the nervous child, has now written with great insight and sympathy on the problems of the nervous child at school. Fatigue and unhappiness at school stand in the constantly changing relation of causes and effects. Among other causes of fatigue attention is drawn to exhaustion by excitement of the carbohydrate reserve, as a result of which the body draws on the fat, and so acidosis is prone to follow; the almost routine use of glucose in cases of fatigue has given good results in the author's practice, but it should be given between, not instead of sugar at meals. There is not any special virtue in glucose which other sugars do not possess, but it is not very sweet and so can be given in a concentrated form without making the drink sickly. The disorders of conduct and of health associated with fatigue are fully considered, and as one of special importance enuresis is dealt with in another chapter. This is a book which not only medical practitioners but also schoolmasters and parents would do well to read and inwardly digest.

Physical Signs in Clinical Surgery. By HAMILTON BAILEY, F.R.C.S. Fourth edition. Bristol: John Wright and Sons, Ltd., 1933. Pp. 287. Illustrations 335 (20 in colour). Price 21*s.*

THE success of this very practical handbook by Mr. Hamilton Bailey shows how greatly appreciated it has been, not only by medical students, but also by practitioners. Its chief virtues are its clear and concise teaching and the excellent illustrations showing how the clinical tests should be carried out—in fact it is no exaggeration to say that no surgical textbook published anywhere in the world is better illustrated than this book. We note that in the new preface the author states, in reply to inquiries, that all the photographs have been taken in the wards or out-patient departments, mostly by his wife or himself, with an ordinary half-plate camera. We congratulate both author and publishers on an outstanding publication.

Simple Instructions for Diabetic Patients. By DOROTHY HARE, M.D., M.R.C.P. London: H. K. Lewis & Co., 1933. Pp. 20. Price 1*s.*

THIS little pamphlet is thoroughly practical and will be invaluable in helping patients and saving the time of their medical attendants and nurses. It points out that the treatment consists mainly in diet, that a patient with true diabetes mellitus can never again take an ordinary diet with safety, and gives the three golden rules: keep to the diet, weigh regularly, and take special care when ill. In clear language directions are given about the way in which insulin should be injected, and how to avoid the unpleasant symptoms due to hypoglycæmia, which may occur three to five hours after an injection of insulin if food has not been taken in the interval.

The Arches of the Years. By HALLIDAY SUTHERLAND. London: Geoffrey Bles. Pp. vii and 293. Price 10*s.* 6*d.*

DR. HALLIDAY SUTHERLAND has had many experiences in a varied life and his descriptions of them are admirable. He tells many good stories, some against himself, and the accounts of his medical teachers at Aberdeen and Edinburgh will make a special appeal to those who knew these outstanding personalities. But perhaps the most interesting part of this graphic story is that of his adventure as a temporary surgeon in the Royal Navy during the war.

Erratum.—The Editor much regrets that the title of Dr. Leonard Williams' book, *Minor Maladies*, reviewed on page 620, was erroneously given as "Minor Ailments," the title of a somewhat similar work by another author.

NOTES AND PREPARATIONS

THE SPAS OF SCOTLAND

Strathpeffer Spa in Ross-shire, although beyond the Caledonian Canal, is only sixteen hours from London, and is therefore nearer than French or German spas and is without the disadvantage of the channel crossing. Magnificent new sleeping and restaurant cars, both first and third class, make the journey a most pleasant one. The village of Strathpeffer itself stands at an altitude of 150 to 300 ft. above sea-level in a broad valley which opens at its eastern end on to the Cromarty Firth, and is bounded at its western end by the rugged and broken mountains of Ross-shire. Ben Wyvis, rising to a height of 3,429 ft., shelters it on the north. The climate of Strathpeffer is sheltered and sedative but none the less invigorating. It is especially a tonic spa, without being in the least an inclement one. The waters at Strathpeffer may be described as pure sulphur waters, since, unlike those of Harrogate, they contain no salts or chlorides. The Cromartie well is one of the strongest sulphuretted waters in Europe. There is also a chalybeate water which contains thirty parts of carbonate of iron. They have a strong diuretic and mild aperient action. The therapeutic indications for treatment at Strathpeffer are chronic gout and rheumatism, chronic skin diseases, chronic diseases of the digestive system, sluggish portal circulation, congested liver, and neurasthenia.

The health resorts of Pitlochry and Gleneagles, though not strictly spas, have invigorating air and lovely surroundings and are very beneficial for convalescent and nerve cases.

Bridge of Allan Spa in Stirlingshire is pleasantly situated in an open valley of the Ochil Hills beside the Highland border, and stands at an altitude of from 30 to 200 ft. above sea-level. The climate is mild and equable even in the winter months. The beautiful scenery of the Trossachs and Perthshire is within easy motoring distance. The original pump house was erected in 1821. After the war, reconstruction of the spa was undertaken and there is now a pleasant spa establishment adjoining the hotel which is well equipped with modern appliances for the usual spa treatments. The waters are chiefly remarkable for the unusually large proportion of calcium which they contain and for the presence of bromine. Their internal action is mildly aperient, alterant and strongly diuretic. They are recommended for catarrhal and hepatic dyspepsia and defective assimilation, chronic gouty and rheumatic affections, and for chronic respiratory catarrhs, both in children and older subjects. Bronchial asthmas have also done well on inhalation treatment with the nebulized water. Under the direction of Dr. Phyllis Lunn and the local practitioners, scientific investigation into the value of modified fasting treatment is being begun. Bridge of Allan may also be safely recommended as a pleasant, sheltered resort both in summer and winter for invalids, the aged and the infirm.

In these days of economic stress and European disturbance the Scottish spas have an unusual opportunity of becoming better known to the British public and to the medical profession.

CARBOSERIN

Carboserin is a preparation of tablets of vegetable charcoal, which is stated by the manufacturers, Messrs. Bayer Products, Ltd. (19 St. Dunstan's Hill, London, E.C.3) to be prepared by a special process which ensures a very high state of activity as compared with ordinary charcoal—by the methylene blue test the adsorbent power of carboserin is 40 times greater than that of ordinary charcoal. Charcoal has, of course, long been known as valuable in the treatment of flatulent dyspepsia. By its adsorbent property, when brought into contact with decomposing matter, oxygen is released and hastens the oxidation of the putrefying matter, while the gases arising from the bacterial action are taken up by the charcoal.

"SOLUBES" TANNIC ACID

The method of treating burns by tannic acid, introduced by Davidson, is now well known and has been accepted as a considerable advance in treatment. One of the difficulties has been to have at hand a supply of the tannic acid solution, which must be fresh, and Messrs. Martindale (12 New Cavendish Street, London, W.1) are now supplying soluble tablets for this purpose. Each "solube" dissolved in 2 oz. of water gives a 2 per cent. tannic acid solution, and with hot water a perfectly clear solution is obtained in one minute. Each "solube" contains 17½ grains of tannic acid, and, also, as has been advised recently (*British Medical Journal*, March 18, 1933, i, 447), ½ grain of mercury perchloride.

ACADEMIC STOCKINGS

Academic stockings are rubberless elastic stockings made for the support of swollen legs and ankles and varicose veins, and they are undoubtedly a great relief to many patients. These stockings are of good texture and colour, which makes them quite invisible even under silk stockings and they are washable. An important feature is the patented heel, which increases the longitudinal tension of the stocking, allowing a very strong pull upwards, and always retains its correct position. They can be obtained in various sizes from retailers, the wholesale distributors being "Academic" Depot, 158/162 Oxford Street, London, W.1.

L'ORIENTATION MEDICALE

L'Orientation Médicale is a monthly review of medical and literary interest, published by Laboratories Lobica, the Paris house of Messrs. Continental Laboratories, Ltd. (30, Marsham Street, London, S.W.1). Although this journal is in the nature of a "house organ" this fact is not obtrusive, and the March number contains, in addition to an article on Malta fever, by Dr. Louis Ramond, articles of general interest. The London branch of the firm will send a copy to any practitioner in this country who will send them his name and address.

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